Diseases Transmitted *from* Animals *to* Man

Third Edition

Diseases Transmitted *from* Animals *to* Man

By

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Charles C Thomas Publisher

Springfield Illinois

Published by Charles C Thomas
at Bannerstone House
301-327 East Lawrence Avenue, Springfield, Illinois

Published simultaneously in Canada by
The Ryerson Press, Toronto

First Edition, January 1950
Second Edition, February 1951
Third Edition, March 1952

Printed in the United States of America

PREFACE TO THE THIRD EDITION

The diseases which animals may transmit to man remain of interest to the veterinarian and the physician the research worker and the health official Each is engaged with a different phase of the problem and views the subject from a different angle The third edition as was the first is presented with each of them in mind to afford a common meeting ground where each may understand the problems of the others and thus through concerted effort reduce the number of infections which man contracts from animals

An attempt has been made to present each disease against a brief historical background emphasizing its epidemiology and means by which infection may be prevented Sufficient bacteriology pathology and clinical symptoms have been included to balance the other material

Certain diseases such as bovine tuberculosis and glanders have lent themselves to control measures and have practically ceased to exist as menaces to man in the United States Other diseases on the other hand have increased in importance During the Second World War much information has been obtained concerning the spread and control of the rickettsial and virus diseases New chapters on these subjects include tsutsugamushi disease Q fever jungle yellow fever lymphocytic choriomeningitis and milkers nodules Other new chapters have been added on listerellosis and Haverhill fever Practically all the old chapters have been rewritten or markedly revised The arthropod borne encephalitides have been combined into one chapter

Appreciation is here expressed to the various contributors who have helped in the preparation of the third edition An acknowledgement has been made at the beginning of the chapter which each prepared In the first and second editions other persons made contributions some portions of which are carried over into the third edition Appreciation is likewise expressed to them especially Drs G M Dack Edward Francis W D Frost G W McCoy and Fred W Tanner My own activities during the past years have curtailed to some extent opportunities for personal observations and asso

PUBLISHED BY CHARLES C THOMAS
AT BANNERSTONE HOUSE
3[illegible]-32[illegible] EAST LAWRENCE AVENUE SPRINGFIELD ILLINOIS

Published simultaneously in Canada by
THE RYERSON PRESS TORONTO

First Edition January 1930
Second Edition February 1931
Third Edition March 193[illegible]

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ciations with animals and animal disease With the assistance of the contributors mentioned however an attempt has been made to present the latest information concerning a very diversified group of diseases

THOMAS G HULL

Chicago Illinois

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'THE WOLF DISARMED OF FEROCITY IS NOW PILLOWED IN THE LADYS LAP THE CAT THE LITTLE TIGER OF OUR ISLAND WHOSE NATURAL HOME IS THE FOREST IS EQUALLY DOMESTICATED AND CARESSED THE COW THE HOG THE SHEEP AND THE HORSE ARE ALL FOR A VARIETY OF PURPOSES BROUGHT UNDER HIS CARE AND DOMINION

EDWARD JENNER LONDON 1796

SECTION ONF

DISEASES OF DOMESTIC ANIMALS AND BIRDS

CHAPTER I

TUBERCULOSIS *

The transmissibility of tuberculous infections to other than natural hosts constitutes one of the most important problems in the control of this ubiquitous disease The ability of the respective pathogenic species of *Mycobacterium tuberculosis* to infect naturally one or more heterologous hosts makes tuberculosis in any species of animals a potential threat to others including human beings, The fact that the organism of cattle tuberculosis is capable of infecting a diversity of species such as swine cats dogs canaries parrots and human beings emphasizes the necessity of a comprehensive plan if tuberculosis is to be successfully controlled or eradicated Likewise the human type of the tubercle bacillus is capable of inducing tuberculosis in cattle swine dogs and parrots The organism of avian tuberculosis in addition to being pathogenic for most birds is capable of causing widespread destructive tuberculosis in swine and sheep These facts make it evident that to eliminate tuberculosis in one species and ignore the disease in others is not likely to solve the larger problem Unless tuberculosis is eliminated in all species it is possible for the disease to exist in heterologous hosts in which the presence of tubercle bacilli constitutes a potential source of new infection perhaps for natural hosts

Natural occurrence of tuberculosis in most of the warm blooded mammals and fowls and in such cold blooded animals as alligators iguanas turtles frogs fish and snakes makes it evident that few if any species of animals have an absolute resistance to the disease Furthermore individual resistance or susceptibility to tuberculous infections varies within wide limits and this fact should be taken into consideration before one draws conclusions as to whether a given species is susceptible to infection with one or more of the several bacterial types of the causative organism

* Prepared by William H Feldman D V M M Sc D Sc Division of Experimental Medicine Mayo Foundation Rochester Minn

features in common there exist sufficient differences by which characteristic representatives of the three types may be distinguished from each other The distinguishing features may be observed by the cultural behavior of the three types by tests of pathogenicity and to a lesser extent antigenically Distinctions based on alleged morphologic characteristics of the three bacillary types of the tubercle bacillus observed microscopically do not constitute reliable criteria for distinguishing one type from another

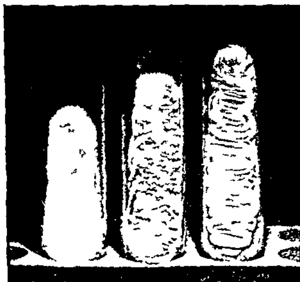


FIG 1 —Slant cultures representative of three types of *Mycobacterium tuberculosis* From left to right the types are bovine human and avian (From Feldman W H Avian tuberculosis infections Baltimore Williams & Wilkins Company 1938)

Culturally on solid mediums the essential characteristics of the three bacillary types of the tubercle bacillus may be summarized briefly as follows

Human Type —This type is glycerophilic Growth is dry crumbly wartlike or cauliflower like Colonies are yellowish The growth is membranous has a roughened surface and may be luxuriant

Bovine Type —Most strains are nonglycerophilic on original isolation They grow much more slowly than the human type the culture

no significance in the production of tuberculosis in the higher mammals, including human beings Additional information regarding the relationship of the [illegible] bacillus to other pathogenic acid fast bacilli has been contributed by Bro[illegible]

Those confronted with the multiplicity of problems which so uniquely characterize tuberculosis should be familiar with the pathogenesis of the different types of the causative agent their natural as well as their heterologous hosts and the means of distinguishing one type from the others The relative susceptibility of different species of animals to each of the types of tubercle bacilli responsible for natural acquired tuberculosis in warm blooded animals is shown in table 1

ETIOLOGIC AGENT *

The causative agents responsible for tuberculosis belong to the genus Mycobacterium and are single celled rod shaped microorganisms that when properly stained have the distinctive characteristic of retaining the stain in the presence of acids diluted in alcohol This acid alcohol fast property while possessed by certain of the higher bacteria molds and actinomyces, constitutes the most distinguishing feature of the bacteria that are known generally as tubercle bacilli and which are responsible for tuberculous diseases in the various species of animals including human beings

The genus Mycobacterium may be conveniently divided into three categories (*1*) species that are pathogenic for warm blooded animals (*2*) species that are parasitic and pathogenic for cold blooded animals and (*3*) species that are saprophytic The saprophytic species are widely distributed in nature especially in soil and are of importance to the student of tuberculosis since they may be confused with pathogenic species of mycobacteria Since we are concerned here primarily with tuberculosis as it affects warm blooded animals we may limit our consideration of the genus Mycobacterium to the following varieties *Mycobacterium tuberculosis var hominis* the natural host of which is human beings *Mycobacterium tuberculosis var bovis* the natural host of which is cattle and *Mycobacterium tuberculosis var avium* responsible for tuberculosis of fowl †

While the various types of tubercle bacilli have certain biologic

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* For those interested in detailed descriptions of the various species of the genus Mycobacterium that are pathogenic for warm blooded animals the following may be consulted Smith (1) Griffith and Munro (2) Topley and Wilson (3) Hagan (4) and Rich (5)

† In 1937 Wells (6) of England reported a disease of wild voles (*Microtus agrestis*) which is due to a previously undescribed acid fast bacillus The disease produced by this organism resembles tuberculosis closely and Brooke (7) suggested *Mycobacterium tuberculosis var muris* as a suitable name for this Mycobacterium The organism is avirulent for guinea pigs and rabbits in moderate doses and so far as is known it is of

criteria for at least preliminary classification As has been shown by Griffith and Munro (2) by Stadnichenko Sweany and Kloeck (8) and by others it is possible by the use of glycerinated and nonglycerinated mediums to distinguish with relative accuracy the bovine and human types of tubercle bacilli The fact that most of the typical human strains are eugonic (grow readily and luxuriantly) while the majority of bovine strains are dysgonic (grow rather poorly) is an important difference in the two types of mammalian tubercle bacilli However the failure of most bovine strains to grow in original isolation in the presence of glycerin while the human type of the organism prospers on mediums containing this substance is of the utmost importance in distinguishing the two types by cultural methods For this reason all materials suspected of containing bovine tubercle bacilli should be cultured in both glycerinated and nonglycerinated mediums

Strains classified as bovine or as avian as a result of cultural differences and physical appearance must be subjected to tests of virulence in suitable laboratory animals if unequivocal proof of bacillary type is to be established Only by determining the susceptibility of guinea pigs rabbits and chickens for a given strain of tubercle bacilli can acceptable evidence of its bacillary type be obtained It must be recognized however that occasionally there are encountered strains that do not possess the requisite characteristics to permit their definite classification as bovine human or avian strains Such strains frequently have the physical appearance of one or the other of the recognized bacillary types of tubercle bacilli but fail to express the degree of virulence for rabbits guinea pigs or chickens that is necessary to establish their exact identity Such strains must be recognized as being of reduced virulence or as being atypical and their true identity cannot be determined by present methods *

The procedure for determining the bacillary type of tubercle bacilli by tests for virulence requires that young cultures representing if possible the original isolation growth be used A weighed amount of the culture should be evenly suspended in sterile physiologic solution of sodium chloride † For convenience in making sub

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* The question of atypical strains of tubercle bacilli has been discussed by Price (9) by Rich (5) and by Stadnichenko Sweany and Kloeck (8)

† Miscibility of bovine and human strains of tubercle bacilli may be facilitated by the addition of a few drops of sterile ox bile to the weighed cells just prior to grinding in the mortar

is of more delicate character, moist, glistening and slimy Growth is seldom luxuriant and is nonchromogenic when the organism is originally isolated

Avian Type —Growth is moist unctuous, slimy and luxuriant It is relatively rapid when compared with the slow growth of the two mammalian types This variety grows well both with and without glycerin and eventually the growth becomes ochroid

Mycobacterium tuberculosis is strictly aerobic and the organism grows best in mediums containing eggs or potato The optimal temperature for the growth of human and bovine tubercle bacilli is 37 5 C while the avian variety of the organism grows best at 40°C The growth characteristics of the three types of tubercle bacilli responsible for tuberculosis in warm blooded animals when grown on solid medium are illustrated in figure 1

Other essential differences between human bovine and avian tubercle bacilli are summarized in table 1

Table 1 —Summary of Some Important Differences Between Avian Human and Bovine Forms of Tubercle Bacilli

Characteristic	Avian	Human	Bovine
Growth in liquid medium	Pellicle formation with crumbly granular growth at bottom	Pellicle formation with growth limited to surface	Pellicle formation with growth limited to surface
Miscibility with saline solution	Suspension easy Organisms uniformly distributed	Suspension difficult Organisms form clumps	Suspension difficult Organisms form clumps
Tuberculin sensitivity	More intense for homologous than for heterologous tuberculin	More intense for mammalian than for avian tuberculin	More intense for mammalian than for avian tuberculin
Pathogenicity	Virulent for chickens and rabbits Slightly pathogenic for guinea pigs	Nonpathogenic for chicken Markedly virulent for guinea pig but only slightly so for rabbits	Nonpathogenic for chicken Markedly virulent for guinea pigs and rabbits

When testing tubercle bacilli for pathogenicity chickens and rabbits should be inoculated intravenously guinea pigs subcutaneously

DETERMINATION OF TYPE

As mentioned previously the physical characteristics of typical human, bovine and avian strains of tubercle bacilli vary sufficiently under proper conditions of artificial cultivation to provide important

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The procedure for determining the bacillary type of tubercle bacilli by tests for virulence requires that young cultures representing if possible the original isolation growth be used A weighed amount of the culture should be evenly suspended in sterile physiologic solution of sodium chloride † For convenience in making sub

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sequent dilutions the relation of the amount of fluid to the bacteria should be adjusted so that 1 c c of the suspension represents 1 mg of bacteria From the original suspension dilutions containing 0 1 mg and 0 01 mg are prepared

The standard test animals for typing tubercle bacilli are guinea pigs rabbits and chickens It is essential that the animals used be free from naturally acquired tuberculosis This is of the utmost importance While naturally acquired tuberculosis is of rare occurrence in guinea pigs and rabbits the same is not true for chickens In many parts of the United States tuberculosis of chickens is exceedingly prevalent a fact which has not always been taken into consideration by some workers who have reported the occurrence of avian tuberculosis in human beings It should be the rule of every laboratory that *no chickens should be used for virulence tests for acid fast bacilli unless the chickens have failed to react to an intracutaneous injection of avian tuberculin* * When possible it is preferable to use young rather than old birds

Each typing series of animals should consist of at least two guinea pigs two rabbits and two chickens Each guinea pig should receive subcutaneously 0 1 mg of the bacterial cells The rabbits and chickens should be inoculated intravenously, each animal receiving 0 01 mg of the bacteria The guinea pigs should be killed for necropsy eight weeks after inoculation, unless they have succumbed before this time Rabbits and chickens living after ninety days should be killed for necropsy

The results of the test for virulence may be interpreted with confidence if one keeps in mind the susceptibility of the respective species inoculated to the bovine human and avian forms of the tubercle bacillus

Briefly the salient facts may be stated as follows Guinea pigs are markedly susceptible to both the human and bovine types of tubercle bacilli but have a high resistance to avian tubercle bacilli Rabbits are highly susceptible to the bovine and avian forms of the organism but have a very limited susceptibility to the human type of the bacillus Chickens have a high susceptibility to the avian tubercle bacillus but have a formidable resistance to the forms responsible for human and bovine tuberculosis Differences in the results of tests of virulence that distinguish the respective acid fast bacilli

* The procedure for conducting a tuberculin test in chickens has been described by Feldman (10)

responsible for tuberculosis in warm blooded animals are summarized in table 2

Table 2—Relative Virulence for Laboratory Animals of the Four Types of Mycobacteria Responsible for Tuberculosis of Warm Blooded Animals

Bacillary Type	Animal			
	Guinea pig	Rabbit	Chicken	Vole
Human	+	∓	0	0
Bovine	+	+	0	+
Avian	∓	+	+	0
Vole	0	0	0	+

Explanation of symbols
0 = Very resistant
∓ = Slightly susceptible
+ = Definitely susceptible

Finally when one is interpreting the results of a typing study by tests of virulence it must be emphasized that typical strains of tubercle bacilli when inoculated into susceptible animals produce progressive disease usually with widespread dissemination of the process to the organs of predilection An alleged bovine strain that produces only localized lesions in guinea pigs and only minimal foci in the lungs of rabbits lacks the virulence necessary to qualify as a bovine form of the organism regardless of its cultural characteristics Likewise an alleged avian strain of tubercle bacilli that does not produce widely disseminated progressive disease in rabbits and in previously tuberculin negative chickens cannot be accepted as a representative of the avian species Identification of types of tubercle bacilli based on morphologic characteristics of the cells physical characteristics of the culture and tests for sensitivity to avian or to mammalian tuberculin must be considered presumptive Convincing evidence of the identification of a given strain can be established only by properly conducted tests of virulence

TUBERCULOSIS OF CATTLE

From the point of view of economic loss hazard to human health and the ubiquitous character of the disease tuberculosis is without question the most important disease of cattle The insidious development of the infection the tenacity of the causative agent and the fact that heterologous hosts are frequently infected provide factors that complicate the control and eradication of tuberculosis of cattle

Incidence—While precise information regarding the true inci

dence of tuberculosis of cattle in the various countries is not available sufficient data are at hand to justify the belief that the disease is distributed throughout the civilized world The incidence in different countries varies greatly depending on (1) the type of animal husbandry practiced (2) the commercial exchange of cattle from one country to another without proper regulatory supervision and (3) the presence or absence of a militant and effective veterinary program of eradication and control In broad geographic terms the greatest concentration of tuberculosis in cattle occurs in the so called low countries of Western Europe including England and Scotland and the lowest incidence is to be found in the United States

According to a report (11) dated 1942 about 40 per cent of the cows of Great Britain are infected with bovine tuberculosis and furthermore the annual loss from this disease due to replacements in the herd condemnation of meat and loss of productivity amounts to about £3 000 000 ($12 000 000) Of ominous significance to human health is the report in 1937 that in Great Britain five of every 1 000 dairy cows eliminate tubercle bacilli in the milk (12) More recently in 1938 Griffith (13) reported that the prevalence of tubercle bacilli in the milk of dairy cows in Great Britain when determined by guinea pig inoculation tests varied from 1 or 2 per cent to as high as 18 per cent

There can be no doubt that bovine tuberculosis constitutes the most serious problem confronting the dairy industry of Great Britain Pasteurization so far as practiced has reduced the danger to human beings from the ingestion of milk from tuberculous animals However this safeguard is generally not applicable to the rural population and ignores the more important and fundamental aspect of the problem which is the source of the infection

In France as in other countries of Western Europe tuberculosis of cattle is exceedingly prevalent The highest incidence of infection occurs among dairy cattle maintained under conditions of permanent stabling According to Van Es (14) tuberculin tests made between 1904 and 1921 of cattle supplying milk for Paris revealed the presence of tuberculous infections ranging from 21 2 to 41 75 per cent What the incidence of tuberculosis in cattle may be at the present time in France is problematic It is likely that the disease is still widespread and its control remains an important unsolved problem

In contrast with England and Scotland where tuberculosis of cattle is rampant the incidence of the disease in Finland is strikingly low According to Pikkarainen (15) the incidence in 1936 was 2 4 per cent and in 1938 it had been reduced to 0 1 per cent Meager data concerning the prevalence of tuberculosis of cattle in northern Italy indicate that cattle are commonly infected with this disease De Gara (16) who reported in 1942 on the occurrence in Italy of the bovine type of infection in human beings emphasized the danger of drinking raw milk and mentioned that in one series thirty seven (6 8 per cent) of 544 samples of market milk contained tubercle bacilli The same author quoted Casco as having found bovine tubercle bacilli in seven of nine specimens of bovine feces and in two of nine specimens of saliva of bovine animals From data available in 1929 Van Es gave the average incidence of tuberculosis among cattle of Germany as 25 per cent Information concerning the prevalence of tuberculosis of cattle in Africa is meager In 1940 Carmichael (17) mentioned that in the District of Ankole Uganda the infection among cattle had reached serious proportions as many as 70 per cent of the animals in different herds reacting to tuberculin *

That tuberculosis occurs among the cattle of India is evident from the report in 1942 of Mallick Aggarwal and Dua (19) In a survey of Amritsar it was found that 25 per cent of 1 234 dairy cattle reacted to tuberculin

In 1941 Webster (20) reported on the prevalence of tuberculosis among cattle in the territory contiguous to Melbourne Australia In 1930 and 1931 some ninety dairy herds containing about 3 000 animals were tuberculin tested and 7 41 per cent reacted In 1939 and 1940 among 28 000 cattle tested comprising 727 herds the incidence of infection was found to be 2 8 per cent

According to Vaccarezza and Arena (21) the rate of tuberculous infection in cattle in Argentina is high In 1941 more than 22 000 000 pounds (10 000 000 kg) of meat were condemned on account of tuberculosis in national slaughtering establishments In Buenos Aires 25 to 40 per cent in La Plata 15 to 25 per cent and in Cordoba 12 2 per cent of the samples of raw milk contained tubercle bacilli Fortunately in these areas it is the general practice to boil milk intended for human consumption

* For additional information on the occurrence of tuberculosis among cattle indigenous in the tropics see an earlier report by Carmichael (18)

In Canada although tuberculosis of cattle is exceedingly prevalent in some of the provinces the disease in most of the Dominion is gradually being brought under control In a report by Cameron (22) it was stated that a third of the cattle of Canada are under official supervision for the control of tuberculosis and that practically all cattle supplying milk to the larger cities have been tuberculin tested At the time of Cameron s report in 1938 it was believed that the incidence of bovine tuberculosis in Canada did not exceed 3 per cent Cameron mentioned the variability of the incidence in the various provinces and disclosed the rather startling fact that in New Brunswick and in Prince Edward Island 100 per cent of the cattle were reactors to tuberculin Obviously in an area where the concentration of infection is so great the public health aspect of the problem assumes very significant proportions

In the United States tuberculosis in cattle has become a relatively rare disease Although the incidence of bovine tuberculosis for the country as a whole was never as high as in many other parts of the world in some areas of the United States the infection was formerly present to an alarming degree According to Russell and Hastings (23) in 1901 the incidence of tuberculosis among cattle as determined by the tuberculin test varied from 4 to 50 per cent The highest incidence occurred among the dairy herds where dairying was practiced most intensively while the range herds were practically free of the infection

As a result of the concerted and militant plan of eradication set up co operatively between the respective states and the Federal Government in 1917 the United States has at the present time probably less tuberculosis of cattle than any other country in the world According to Wight (24) * 8 105 480 cattle were tuberculin tested during the fiscal year ending June 30 1945 These cattle represented 484 749 herds located in the various states and Hawaii the Virgin Islands and Puerto Rico The percentage of cattle reacting to the tuberculin test was 0 24 Indicative of the paucity of tuberculosis among dairy and breeding cattle in the United States at the present time are further data reported by Wight which show that of 147 346 dairy and breeding cattle tuberculin tested during the fiscal year 1944 to permit interstate shipment only ten were reported as reactors

* Chief Tuberculosis Eradication Division United States Department of Agriculture

Further evidence of the low incidence of tuberculosis in cattle in the United States is given by the figures of the meat inspection service of the United States Department of Agriculture representing animals other than tuberculin reactors that were slaughtered for food at Federally supervised establishments during the fiscal year 1945 Among a total of 14 504 806 cattle slaughtered, lesions considered tuberculous were found in 5 830 (0 04 per cent) Only 1 380 (0 01 per cent) of the carcasses were condemned and 159 carcasses were passed for human consumption after thorough cooking

The remarkable diminution in the incidence of tuberculosis among cattle in the United States has been achieved by the ruthless application of the one sure method of eradicating tuberculosis among domesticated animals—the tuberculin test and the slaughter of the reactors * According to Wight (26) since the tuberculosis eradication plan was initiated in 1917 a total of 279 235 490 cattle have been tested with tuberculin up to June 30 1945 The number of animals that reacted to the tuberculin test was 3 891 950 The total amount of money expended to accomplish this stupendous and important task including funds appropriated by the counties states and Federal Government was approximately $250 000 000 Considering the results achieved the cost has not been excessive That the task could be accomplished provides truly an amazing example of man s ability to utilize the knowledge of science by integrating the efforts of the veterinary and the medical professions to free his environment of formidable and insidious factors that threaten his life and economic well being However the gains made in controlling bovine tuberculosis can be advanced or maintained only by recognition of the fact that constant vigilance is necessary As long as a single tuberculous animal exists the possibility of the transmission of the infection to healthy animals and to human beings exists The goal should be complete elimination of the disease

The Pathology of Tuberculosis of Cattle †—It is the opinion of those who have investigated the pathogenesis of tuberculosis of cattle that in adult animals the infection in the majority of instances is primarily in the lungs and that the tubercle bacilli reach the parenchyma of the lung by way of the respiratory tract (1 28 29 30)

* For a detailed and interesting account of the attack against bovine tuberculosis the reader should consult the book by Myers (25)

† Limitation of space does not permit a detailed account of the pathology of tuberculosis for additional information see Van Es (14) and Hutyra Marek and Manninger (27)

In suckling calves according to Nieberle most of the primary infections occur in the gastro intestinal tract (including the contiguous lymph nodes) In Nieberle s series of 100 suckling calves the primary focus occurred in the lung in 13 per cent of the animals *



FIG 2—Multiple caseocalcareous tuberculous nodules in the lung of a bovine (Courtesy of Dr Harry W Schoening Bureau of Animal Industry United States Department of Agriculture)

Being in most instances a chronic progressive disease tuberculosis causes destruction of the tissues in the immediate vicinity of the original focus and may become caseous fibrocaseous cavitating or calcareous (fig 2) From the softening destructive primary focus spread to adjacent regions by continuity or to distant situations by hematogenous means frequently occurs As a consequence no tissue of the animal is immune to the formation of tuberculous lesions although the sites of predilection are lungs liver spleen serous membranes and kidneys (fig 3) Rarely the musculature is affected †

* According to Stamp (30) in 1944 Nieberle (28) expressed the opposite point of view stating that pulmonary infection in the calf is much more frequent than alimentary infection

† The question of tuberculosis of the musculature of cattle is considered on p 38

In addition and of great importance to human health the parenchyma of the udder may be the site of tuberculous foci from which infectious material finds its way into the milk * (fig 4) In the



Fig 3—Extensive pleural and peritoneal lesions of tuberculosis in carcass of a dairy cow (From Van Es L Bovine tuberculosis Circular 23 University of Nebraska College of Agriculture Experiment Station Lincoln Nebraska Revised 1929)

udder the disease may affect all four quarters The supramammary lymph nodes may or may not be involved † The disease may be chronic or acute and invariably leads to extensive tuberculous involvement of the duct system (fig 5) As Stamp (31) pointed out in all cases of tuberculosis of the bovine udder the lesions are open and sufficient functioning lactating lobules persist to provide for the secretion of at least some milk which of course invariably contains tubercle bacilli Although the disease is transmitted to the udder by the blood stream local spread through the duct system probably *occurs in all cases In practically all instances the excretion of tuber*

* For an admirable description of tuberculosis of the bovine udder see the report of Stamp (31)

† According to Stamp (31) the involvement of the supramammary lymph nodes does not indicate that the udder is tuberculous In fact the condition of the supramammary lymph nodes according to Stamp is of no diagnostic value in detecting tuberculosis of the bovine udder

cle bacilli in the milk denotes demonstrable lesions in the udder However Topley and Wilson (3) pointed out that tubercle bacilli may occur in the milk without demonstrable gross or microscopic lesions in the mammary gland Whether tubercle bacilli can actually pass through the intact tissues of the parenchyma of the udder should be subject to investigation It seems more likely that when

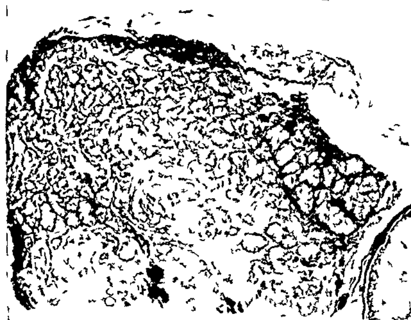


FIG 4 —Extensive and severe tuberculous involvement of the udder There has been considerable destruction of the parenchymal tissues which have been replaced largely by caseocalcareous lesions of tuberculosis (Courtesy of Dr Harry W Schoening Bureau of Animal Industry United States Department of Agriculture)

the organisms are present in milk as it is drawn from the udder alterations of tissue are present even though they may be exceedingly difficult to find

The fact that bovine tuberculosis when in a progressive state causes destruction of tissue which may cause the morbid process to break through into channels leading to the exterior of the body provides an important circumstance favorable to the transmission of the disease to other animals and to human beings Lesions of the lungs may ulcerate into the bronchi and tubercle bacilli be eliminated with the expired air during coughing or the bacilli may be

swallowed with mucous secretions and subsequently be eliminated with the feces * Tuberculosis of the kidney may cause sufficient destruction to permit the discharge of infectious material into the renal pelvis and hence egress with the urine In tuberculosis of the testes the semen may be infected and if the disease affects the reproductive organs of the female the vaginal discharges are likely to contain tubercle bacilli If the disease is present in the intestinal mucosa or in the liver the organisms find their exit with the fecal discharges

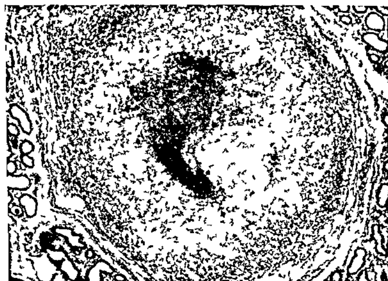


Fig 5 —Chronic nodular tuberculosis of the udder of a cow Minimal calcification has occurred and acid fast bacillary forms were demonstrable among the cellular detritus (x55) (Courtesy of Dr J S Bengston Bureau of Animal Industry United States Department of Agriculture)

To recapitulate In tuberculous cattle the infective bacteria may occur in a variety of materials excreted or secreted by the infected animal These materials include discharges from the respiratory tract milk urine semen vaginal discharges and feces If infected any and all of these may serve as a medium for the transmission of tuberculosis to previously noninfected hosts *From every point of*

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* In a study of feces from 391 apparently healthy cows in five counties in England Williams and Hoy (32) demonstrated tubercle bacilli in the feces of six (1 53 per cent)

view the tuberculous bovine is potentially a highly dangerous animal

TRANSMISSIBILITY OF BOVINE TUBERCULOSIS TO OTHER SPECIES OF HOST

As mentioned previously one of the features of the organism responsible for tuberculosis of cattle is its ability to prosper in certain heterologous hosts in which it may produce consequences as serious as those possible in the natural host

Transmissibility Cattle to Human Beings—The development of our knowledge concerning the virulence for human beings of the bacillus of bovine tuberculosis has been slow and has frequently been interrupted by the temporary acceptance of opinions to the exclusion of facts Several years before Koch (33) announced the discovery of the tubercle bacillus in 1882 Villemin (34) proved by animal experimentation that tuberculosis is a contagious disease and is the effect of a specific causative agent Twenty five years after Koch s discovery the danger to human beings of milk from tuberculous cattle was generally accepted This point of view was influenced considerably by Koch s (33) statement made at the time he reported the discovery of the tubercle bacilli that bovine tuberculosis is identical with the disease in man and is thus a disease transmissible to man

At the British Congress on Tuberculosis held in London in 1901 Koch (35) reversed his former position and said in effect that human tuberculosis differs from that of cattle and cannot be transmitted to bovines * Furthermore Koch held the view that the susceptibility of human beings to bovine tubercle bacilli is uncertain and if infection of human beings with the bacillus of bovine tuberculosis occurs it must be very rare Finally he said I should estimate the extent of infection by the milk and flesh of tuberculous cattle and the butter made of this milk is hardly greater than that of hereditary transmission and therefore do not deem it advisable to take any measures against it

Koch s point of view as to the unimportance of the bovine tubercle bacillus as a hazard to human health was opposed by the officials of the London Congress This opposition was shared by many eminent scientists who attended the Congress including Lord

* Smith (36) in 1898 reported the results of his studies that had established definitely differences between human and bovine tubercle bacilli

Lister and at a general meeting of the Congress Ravenel (37) reported the first recorded instance of having isolated from a human being a tubercle bacillus that was proved to be of the bovine variety *



FIG 6 —Pulmonary tuberculosis of the right lung of a young woman due to the bovine variety of the tubercle bacillus The patient had worked for several years as a dairy maid, starting at the age of fourteen years Both lungs were extensively affected (From Myers J A Man's Greatest Victory Over Tuberculosis Springfield Illinois Charles C Thomas 1940)

* As a matter of fact Ravenel (37) reported at the Congress five cases of probable bovine tuberculosis in human beings one patient was Ravenel's laboratory assistant three patients were veterinarians and one was a cattle car cleaner The disease in all but one case was localized Later Ravenel reported before the Pathological Society of

The question of virulence of bovine tubercle bacilli for human beings became so pertinent after Koch's address at the London Congress on Tuberculosis that an official agency was formed to ascertain the facts. Thus there came into being the Royal Commission on Tuberculosis. In the several years of its existence the Royal Commission made a noteworthy contribution to the knowledge of tuberculosis. Exhaustive and careful studies were made on cultures of tubercle bacilli obtained from cases of human, bovine and avian tuberculosis and the results constitute a great amount of essential fundamental information that has served as a guide for subsequent workers. The final report of the Commission was issued in 1911.

In an interim report published by the Commission in 1907 the importance of the bacillus of bovine tuberculosis to human beings was emphasized by the following statement: "Cow's milk containing bovine tubercle bacilli is clearly a cause of tuberculosis and fatal tuberculosis in man. Our results clearly point to the necessity of measures more stringent than those at present in force being taken to prevent the sale and consumption of such milk." *

Several members of the British Royal Commission on Tuberculosis continued to explore the problem of the transmissibility of bovine tubercle bacilli for many years after the activities of the Commission had ceased. Among these was the late A. Stanley Griffith, whose persistent and meticulous work and the conservative interpretation of whose results were probably more responsible for the final indictment against the bacillus of bovine tuberculosis as a menace to human health than were the efforts of any other individual.

It is of historical interest to note that, although Koch at the International Congress on Tuberculosis in Washington in 1908 did retreat somewhat from his previous dogmatic insistence that the danger of the bacilli of cattle tuberculosis for human beings is negligible, he did maintain that satisfactory proof of chronic pulmonary tuberculosis in human beings due to bovine tubercle bacilli had not been established.† According to Griffith and Munro only two cases could be quoted at the time (1908) and in one of the cases it appeared likely that human and bovine types of the tubercle

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Philadelphia a case of tuberculous meningitis in a child seventeen months of age from whom tubercle bacilli were obtained and proved by cattle inoculation tests to be of the bovine variety. Smith (1) isolated bovine tubercle bacilli from a child in 1905.

* Quoted from Griffith (38).

† Quoted by Munro and Walker (59).

were both present and consequently valid proof that the bovine tubercle bacillus contributed to the causation of the disease was lacking A few months later in February 1909 Griffith (38) in England obtained unmixed cultures of bovine tubercle bacilli from the sputa of two men twenty one and thirty one years of age respectively In 1913 Griffith isolated (in Edinburgh) bovine tubercle bacilli from a girl sixteen years of age who had pulmonary tuberculosis and in 1916 another instance of pulmonary tuberculosis due to the bovine tubercle bacillus was reported by Wang (40) (also of Edinburgh) the patient being a man forty one years of age

Although Koch eventually modified his views regarding the danger of the bacilli of cattle tuberculosis to human beings the influence of his earlier belief was well entrenched Koch s erroneous views must be held largely accountable for the tragic consequences that ensued from the earlier failure of a more general recognition that bovine tubercle bacilli have a considerable pathogenicity for human beings and are capable of producing in human beings a wide variety of tuberculous infections including pulmonary forms of the disease

The frequency of the bovine type of tuberculous infection in human beings is dependent on the incidence of the disease in cattle and the quantity of raw milk consumed Regardless of the anatomic situation of the resultant disease the most likely source of bovine tubercle bacilli responsible for infection of human beings is one or a combination of the following raw or improperly heated milk from tuberculous cows the products of milk from tuberculous cows contaminated air expired from the lungs of tuberculous cattle or human beings infected with the bovine type of infection In addition it should be recognized that butchers and meat inspectors whose duties expose the unprotected skin of the arms and hands to virulent material when handling tuberculous carcasses are in danger of cutaneous infection Thus the possibility of occupational tuberculosis must be recognized * In fact several cases of bovine tuberculous infection of butchers have been reported by Saenz (42)

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* Hermansson (41) inoculated guinea pigs with water in which a meat inspector had washed his hands after examining carcasses of tuberculous cattle and demonstrated the presence of virulent tubercle bacilli Similar tests showed the presence of tubercle bacilli in the water used by butchers to wash their hands and in the water used to wash towels used by the meat inspector

Table 3.—THE PERCENTAGE OF BOVINE TUBERCULOSIS AMONG CASES OF HUMAN AND BOVINE TUBERCULOSIS IN MAN IN DIFFERENT COUNTRIES OF THE WORLD (DATA COMPILED BY PRICE 43)

COUNTRY	TOTAL	HUMAN	BOVINE	
			Number	Per cent
France	1 083	1 055	28	2.6
Germany	1 165	1 007	158	13.6
Netherlands	767	701	66	8.6
Switzerland	218	201	17	7.8
Sweden	14	14	0	0
Norway	107	101	6	5.6
Poland	160	149	11	6.9
Italy	871	846	25	2.9
Spain	95	90	5	5.3
Hungary	334	328	6	1.8
Greece	327	327	0	0
Australia	280	246	34	12.1
Japan	272	264	8	2.9
United States	1 362	1 202	160	11.7
Canada	901	847	54	6.0

In Italy there were [illegible]4 atypical strains

In presenting evidence incriminating the bacilli of bovine tuberculosis as a cause of tuberculous infections of human beings no attempt will be made to give a complete review of the literature. An admirable review of the subject was published by Price (43) in 1939. Price's review was based on an analysis of reports pertaining to about 18 000 strains of tubercle bacilli studied in various parts of the world. *Her study led to the conclusion that the total proportion of human tuberculosis induced by the bovine tubercle bacillus* is approximately 10 per cent.

This figure, while serving to emphasize the important significance of the virulence of bovine tubercle bacilli for human beings, inadequately incriminates this type of the organism in the over-all picture of tuberculosis in those countries where the opportunities for infection with bovine tubercle bacilli are greatest. As one might expect, there is a definite parallelism in different countries between the incidence of tuberculosis in cattle and the bovine type of tuberculous infection in human beings. Thus the greatest number of reported cases of human tuberculosis of bovine origin have occurred in the British Isles, where, as mentioned previously, about 40 per cent of the cows are tuberculous.* Conversely, the lowest incidence

* Rich (5), in commenting on the high incidence of the bovine type of infection in human beings in Great Britain, wrote, "This well known fact is a sad commentary upon human cupidity." Rich pointed out that 2 000 children die annually in Great Britain from bovine tuberculosis because of the lack of social responsibility on the part

of tuberculosis due to the bovine tubercle bacillus is in the United States where the disease in cattle as indicated by the tuberculin test has been reduced to the low figure of 0.24 per cent

Data on the percentage of bovine tuberculosis among cases of human and bovine tuberculosis in human beings in various countries of the world as compiled by Price are given in table 3 It must be recognized that the figures given in table 3 represent only approximations of the true proportion of bovine tuberculosis in human beings but they provide sufficient evidence to leave no doubt that tuberculosis in cattle is a menace to human health Undoubtedly *the figures indicating the proportion* of bovine tuberculosis in human beings given for the United States (11.7 per cent) are too high so far as the present situation is concerned The most recent reports included in Price's compilation were published in 1933 and the study in which the largest number of bovine infections were found was reported in 1910 (44) The true proportion of human infection with bovine tubercle bacilli in the United States at the present time is problematic but fragmentary evidence suggests that it is ex

Table 4 —PERCENTAGE IN ENGLAND OF THE BOVINE TYPE OF INFECTION AMONG 1,498 CASES OF EXTRAPULMONARY HUMAN TUBERCULOSIS (GRIFFITH 38)

VARIETY OF TUBERCULOSIS OR SOURCE OF MATERIAL	CASES	PERCENTAGE OF CASES IN DIFFERENT AGE GROUPS IN WHICH THE BOVINE TYPE OF BACILLUS WAS FOUND		
		Less than 5 years	5 to 15 years	All ages
Adenitis (cervical)	126	90.9	53.4	50.0
Lupus	191	8.4	44.4	48.7
Scrofuloderma	60	53.3	43.3	36.6
Bone and joint	[illegible]3	29.5	19.1	19.5
Genito-urinary	23	—	—	17.4
Meningeal	265	28.1	24.5	24.6
Necropsies	187	28.6	15.5	27.5
Miscellaneous	23	33.3	9.1	8.7

tremely low especially among children the age group in which the bovine type of infection is most prevalent in European countries

The magnitude of the public health problem which tuberculosis in cattle creates in the British Isles is evident from the information which Griffith (38) compiled in 1937 from the reports of several investigators The data pertaining to England are presented in table 4 while data for Scotland are shown in table 5

of powerful dairy interests which have frustrated all attempts to enact legislation making pasteurization of milk sold to the public compulsory

The data presented in table 4 and table 5 pertain only to extra pulmonary infection due to the bacillus of bovine tuberculosis While the statistics in table 4 and table 5 do not disclose the exact number of cases of the bovine type of infection among patients of fifteen years of age or less it is generally known that the bovine type of tubercle bacilli affects the younger age groups more frequently than it affects adults It is also recognized that infection of human beings with the bacillus of bovine tuberculosis produces in most instances tuberculous cervical adenitis tuberculosis of the skin tuberculosis of the peritoneum or tuberculosis of the bones and joints

Table 5 —PERCENTAGE IN SCOTLAND OF THE BOVINE TYPE OF INFECTION AMONG 873 CASES OF EXTRAPULMONARY HUMAN TUBERCULOSIS (GRIFFITH 38)

VARIETY OF TUBERCULOSIS OR SOURCE OF MATERIAL	CASES	PERCENTAGE OF CASES IN DIFFERENT AGE GROUPS IN WHICH THE BOVINE TYPE OF BACILLUS WAS FOUND		
		Less than years	5 to 15 years	All Ages
Adenitis (cervical)	93	65 0	62 3	51 6
Lupus	13	100 0	71 4	69 2
Bone and joint	218	46 2	28 9	29 8
Genito-urinary	42	—	—	31 0
Meningeal	203	34 4	14 0	29 6
Necropsies	290	33 6	38 5	32 4
Miscellaneous	14	—	—	71 4

While it was recognized that tuberculosis of the bovine type might affect almost any tissue of the body pulmonary disease due to this organism was considered of infrequent occurrence until the important investigations of several workers especially Griffith and his colleagues in Britain and Jensen of Denmark proved the situation to be otherwise (fig 6) According to Griffith (38) up to 1922 only four cases of human pulmonary tuberculosis due to the bovine type of the tubercle bacilli had been established In 1922 Munro found two additional cases among 100 cases of pulmonary tuberculosis studied (38) The latter finding according to Griffith provided an impetus which initiated prolonged and extensive investigations by many workers These studies produced the important information that in countries where bovine tuberculosis is prevalent and where milk is consumed in a raw state so as to provide frequent exposure pulmonary tuberculosis due to the bovine tubercle bacillus may be expected to occur in a small to a considerable percentage of cases

The evidence presented by Griffith and Munro (2) in 1944 con

cerning the role of the bovine tubercle bacillus in human pulmonary tuberculosis is most impressive and belatedly provides an unequivocal answer to Koch s skepticism regarding the ability of this type of the tubercle bacillus to produce pulmonary disease in human beings Griffith and Munro s report was based on a study of 6 963 cases of pulmonary tuberculosis in Great Britain In every instance tubercle bacilli were isolated from the sputum and the bacillary type of each strain was determined by appropriate laboratory procedures Some of the more important findings follow (1) In Scotland among 2 769 cases the percentage of pulmonary infections due to the bovine tubercle bacillus was 5 8 the highest percentage of bovine infections being in the Orkney Islands (25 8 per cent) and the lowest percentage (4 4 per cent) in the city of Aberdeen where it was believed that many of the infections had originated in rural areas (2) Among 3 671 strains of tubercle bacilli obtained from patients in England seventy nine (2 15 per cent) were bovine in origin (3) In Wales the bovine type of infection was found in two of 203 cases while in Eire an examination of 320 cases did not disclose any instance of bovine infection (4) In the series studied a total of 241 cases of pulmonary tuberculosis affecting human beings were due to infection with the bacillus of bovine tuberculosis This figure represents an incidence of 3 5 per cent of the total number of cases investigated (5) The strains from 232 of the 241 cases were fully virulent by animal tests of pathogenicity while nine strains showed varying degrees of attenuation (6) Previous cervical and abdominal tuberculous adenitis and involvement of bones and joints in a considerable proportion of the cases suggested the alimentary canal as the portal of entry of the infection (7) There was no doubt that the great majority of the patients from whom bovine tubercle bacilli were obtained had been infected through the agency of cow s milk (8) In five instances both human and bovine strains of tubercle bacilli were obtained from a single patient (9) The possibility of infection from one human being to another was presumptive in a few instances but not proved (10) Pulmonary tuberculosis in human beings caused by bovine tubercle bacilli was indistinguishable clinically radiologically and by postmortem examination from pulmonary tuberculosis due to tubercle bacilli of the human type (fig 7)

That the bovine type of tubercle bacilli constitutes a problem of major importance in the epidemiology of tuberculosis of human

beings in Denmark is evident from the data presented in table 6 Data obtained from extensive studies of the problem in other North European countries disclose the fact that infection of human beings and especially children by bovine tubercle bacilli is of common occurrence Ruys (45) for example, working among Dutch children



FIG 7—Thorax of a man nineteen years of age who worked on a farm near Lund Sweden There was no tuberculosis in the man s family but the disease was present among the swine and the cattle of the farm where he worked Sputum from this man yielded tubercle bacilli of the bovine type (From Myers J A Man s Greatest Victory Over Tuberculosis Springfield Illinois Charles C Thomas 1940)

from large towns and rural districts who had pulmonary tuberculosis found that in 9 per cent of the cases the disease was due to the bovine type of the bacillus Among adults from large towns who had pulmonary tuberculosis the proportion of bovine infection was 1 per cent while among adults from rural areas the proportion of the bovine type of infection in pulmonary tuberculosis was 6 per cent The proportion of infection due to bovine tubercle bacillus in cases of extrapulmonary tuberculosis was 20 per cent for both rural and urban patients *

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* In another report Ruys (46) mentioned that about 35 per cent of all cattle slaughtered in Amsterdam in 1933 and 1934 were tuberculous and that 40 per cent of 11 000 cattle in the provinces tested with tuberculin reacted positively

During a period of three years Hedvall (47) investigated the occurrence of pulmonary tuberculosis due to the bovine type of the tubercle bacillus among patients in southern Sweden About 3 300 specimens were examined and 746 separate cultures of acid fast bacilli were obtained Sixty five strains were bovine in character The age of the patients who had the bovine type of infection varied from seven months to sixty eight years and the majority lived in rural areas

Lange (48) working at the Robert Koch Institute Berlin determined the type of tubercle bacilli present in the sputa of tuberculous patients who as a consequence of their occupations—milkers veterinarians and butchers—were especially liable to exposure to tuberculous cattle During the years 1927 to 1937 sputa from 171 patients were studied and cultures of acid fast bacilli were obtained from 148 When finally classified by appropriate tests 136 strains of tubercle bacilli of human type were revealed and nine strains of bovine origin were recognized In three of the cases mixed cultures of human and bovine tubercle bacilli were recorded The ages of the patients varied from seventeen to fifty one years

Table 6—Incidence in Denmark of the Bovine Type of Infection Among 2 946 Cases of Human Tuberculosis (Jensen and Frimodt Moller Quoted by Price 43)

Variety of Tuberculosis	All Ages			Less Than 15 Years			15 to 29 Years			30 Years and More		
	Total	Bovine	Per cent	Total	Bovine	Per cent	Total	Bovine	Per cent	Total	Bovine	Per cent
Respiratory	1 824	88	4 8	432	29	6 7	1 007	50	5 0	385	9	2 3
Bone and joint	567	105	18 5	98	24	24 5	255	57	22 4	214	24	11 2
Lymph nodes	251	123	49 0	80	66	82 5	97	47	48 5	74	10	13 5
Meningeal	304	75	24 7	176	58	33 0	92	13	14 1	36	4	11 1
Total	2 946	391	13 3	786	177	22 5	1 451	167	11 5	709	47	6 6

That there was an occupational factor in Lange s series may be inferred from the following Among sixty nine milkers who had pulmonary tuberculosis human tubercle bacilli were present in sixty cases the bovine tubercle bacillus was the causative agent in eight cases and in one case both human and bovine types of the bacillus occurred Among forty patients comprising butchers and veterinarians thirty seven were infected with tubercle bacilli of the human type only one with bacilli of bovine tuberculosis and in two a mixed human and bovine infection occurred In a third group totalling thirty nine patients composed of masons carpenters and

others all infections were found to be due to the human type of the organism Lange quoted the report of Goeters in Leipzig, who obtained at necropsy material from 118 cases of pulmonary tuberculosis and identified the bovine type of infection in six In four of the six cases of bovine type of infection the subjects had been adults

In France although numerous reports leave no doubt of the reservoir of potential infection which exists in the bovine population the incidence of the bovine type of infection in human beings is much lower than one might expect The fact that cow s milk is seldom consumed in France without previously being heated undoubtedly accounts for the relatively low incidence of infection of human beings by the bacillus of bovine tuberculosis In 1939 Saenz (42) reported on the role of the bovine tubercle bacillus in human tuberculosis in France Saenz s data showed that among 903 cultures of tubercle bacilli isolated from various types of clinical tuberculosis among human beings of whom more than a half were children only twenty two (2 4 per cent) were of bovine origin * Except for seven of the cases of bovine infection in which the patients were butchers who presumably were occupationally exposed to the infection in most of the cases of bovine infection the patients were children Saenz also reported on twenty four cases of lupus in only two of which were the lesions due to bacilli of bovine origin and he mentioned that in other countries bovine tubercle bacilli account for 50 per cent or more of the cases of lupus

The occurrence in Italy of infection of human beings by the bacillus of bovine tuberculosis was described in 1942 by de Gara (16) In addition to summarizing the findings of previous investigators de Gara included in his report an account of cases that he had investigated † (table 7) The data shown in table 7 indicate that in Italy the bovine type of infection does not constitute any large part of the problem of tuberculosis as it applies to human beings However the fact that the disease slowly smolders in its natural host makes it a constant menace to at least a certain proportion of the rural population who may live or work in close contact with tuberculous animals and to those who while presumably drinking only cooked or adequately heated milk may forget or disregard

* Not all of the twenty two strains of tubercle bacilli designated as of the bovine type by Saenz were identified by animal inoculation tests which fact provokes certain reservations regarding the true bacillary type of some of the strains

† Work done at the Hygienic Institute University of Milan

this important safeguard Evidently in Italy pasteurization is not practiced except in the larger communities and as a consequence milk is rendered safe by the household practice of boiling it to prevent souring Indicative of the hazard are de Gara s figures showing that tubercle bacilli were found in 6 8 per cent of 544 samples of market milk De Gara stated that more than 1 000 strains of tubercle bacilli had been typed in all Italy and the incidence of the bovine type was found to be 4 8 per cent

Table " —PERCENTAGE OF BOVINE TUBERCULOSIS IN ITALY (DE GARA 16)

VARIETY OF TUBERCULOSIS	TOTAL NUMBER EXAMINED	BOVINE TYPE	
		Number	Per cent
Bone and joint	8	1 (?)	12 5 (?)
Cervical lymph node	27	1	3 7
Other extrapulmonary	217	14	6 5
Pulmonary	6 7	20	3 0
Total	909	36	4 0

Du Toit and Buchanan (49) stated that tuberculosis of cattle is of common occurrence in South Africa However infection of human beings with the bacilli of bovine tuberculosis has rarely been demonstrated Du Toit and Buchanan collected from the literature of South Africa information to the effect that of 242 strains of tubercle bacilli obtained largely from tuberculosis of bones and joints lymph nodes and meningeal lesions only one—that derived from a case of tuberculous meningitis—proved to be bovine in origin

Carmichael (17) who studied pulmonary tuberculosis in the natives of Uganda mentioned a survey by Wilcocks in 1939 in the territory of Tanganyika in which the sputa of sixty seven natives affected with pulmonary tuberculosis were studied and all strains were of the human type Carmichael s own observations include the fact that the cattle of the district of Ankole were severely infected with tuberculosis as many as 70 per cent of the animals reacting positively to the tuberculin test Using cultural methods and the inoculation of rabbits Carmichael determined the bacillary type of 283 strains isolated in cases of pulmonary tuberculosis only four were of the bovine type

Webster (20) reporting in 1941 on the relative incidence of human and bovine types of tuberculosis among the people of Victoria Australia stated that among 183 adults affected with a variety of

others all infections were found to be due to the human type of the organism Lange quoted the report of Goeters in Leipzig who obtained at necropsy material from 118 cases of pulmonary tuberculosis and identified the bovine type of infection in six In four of the six cases of bovine type of infection the subjects had been adults

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† Work done at the Hygienic Institute University of Milan

culosis have been identified from pulmonary and extrapulmonary tuberculous disease in Argentina The fact that boiling of milk is generally practiced probably accounts for the apparently low rate of infection of human beings by tubercle bacilli of the bovine type

Indicative of the part that milk from tuberculous cows may have in incapacitating children are the results of a study by Price (9) in Toronto Canada Reporting in 1938 Price had accumulated data during the previous thirteen years on 500 tuberculous children and found that 9 6 per cent of the extrapulmonary tuberculosis was due to the bovine type of infection The youngest child in Price s series was six and a half months of age and without exception the children came from an environment that did not provide for the pasteuriza tion of milk

The most recent investigation in the United States of sufficient scope to provide significant data on the occurrence of tubercle bacilli of the bovine type in human pulmonary tuberculosis was reported by Beattie and Nicewonger (51) in 1942 A total of 366 strains of tubercle bacilli from the sputa of persons in sanatoriums and hospitals in various parts of California were studied The strains were screened by cultural methods and those that were dysgonic or not typically eugonic were subjected to tests for virulence in rabbits No strains considered to be bovine in type were found

Earlier reports on the incidence of infection with bovine tubercle bacilli in human beings in the United States vary as follows Of the 564 cases of tuberculosis reported by Park and Krumwiede (44) in 1910 the bovine type of infectious agent was present in 7 6 per cent In Aronson and Whitney s (52) series and in the report by Van Es and Martin (53) the incidence of the bovine type of infection was 3 8 and 3 9 per cent respectively In 1933 Chang (54) reported the results of a study he had made at a sanatorium in Massachusetts His results indicated that in approximately a fourth of the 200 cases studied the infective organisms were of the bovine type The figures of Chang are definitely unusual and probably do not represent a true indication of the extent of infection of human beings with the bacilli of bovine tuberculosis generally throughout the United States at the present time As a matter of fact it is generally be lieved that at present infection of human beings with the bacilli of bovine tuberculosis is of rare occurrence Perhaps the subject should be investigated further by determining the type of tubercle bacilli present in the sputa of elderly persons who have been infected with

clinical forms of tuberculosis no instance of bovine type of infection occurred Among 123 children, eleven (8 9 per cent) were affected with the bovine type of the tubercle bacillus The tissues affected in the cases in which the bovine form of the organism was the infective agent included tonsils and cervical and mesenteric lymph nodes According to Webster in Victoria the bacillus of bovine tuberculosis has little or no part in the causation of osseous tuber culosis

According to Kimura and Kondo (50) Kitasato was the first in Japan to investigate the role of the bovine type of the tubercle bacillus in human infections A total of 152 cases were studied but in none was the bacillus of bovine tuberculosis recognized Kimura and Kondo summarized the work of various Japanese authors on the incidence of bovine tuberculous infections in human beings in relation to the total number of cases in which determination of the type of infecting organism was made They found as of February 1939 that a total of 1 323 cases of tuberculosis (in all of which the patients were Japanese) had been studied bacteriologically and that the human type of the infecting agent had been present in 1 310 cases while in only thirteen cases (0 98 per cent) were bovine *tubercle bacilli recognized The varieties of tuberculous disease* from which the thirteen strains were obtained consisted of the following lung and pleura one strain bone and joint tuberculosis two strains tuberculous cervical lymph nodes two strains tubercu losis of the genito urinary tract one strain tuberculosis of the skin seven strains The authors attributed the low rate of infection with the bovine type of the tubercle bacillus largely to the fact that the Japanese do not consume as much raw milk as the inhabitants of certain European countries where the rate of infection is many times that for Japan

Although reports indicate that tuberculosis is prevalent among the cattle in Argentina relatively few instances have been reported in which *the bovine type of the tubercle bacillus has been obtained* from tuberculous human beings According to Vaccarezza and Arena (21) the bovine type of infection in human beings was first recognized in Argentina by Ligniers in 1904 The same authors quoted Poire and Arseno-Carranza as having studied 150 strains of tubercle bacilli obtained from the sputa of patients suffering with pulmonary tuberculosis none was bovine in type Vaccarezza and Arena mentioned that in a few instances the bacilli of bovine tuber

culosis have been identified from pulmonary and extrapulmonary tuberculous disease in Argentina. The fact that boiling of milk is generally practiced probably accounts for the apparently low rate of infection of human beings by tubercle bacilli of the bovine type.

Indicative of the part that milk from tuberculous cows may have in incapacitating children are the results of a study by Price (9) in Toronto, Canada. Reporting in 1938, Price had accumulated data during the previous thirteen years on 500 tuberculous children and found that 9.6 per cent of the extrapulmonary tuberculosis was due to the bovine type of infection. The youngest child in Price's series was six and a half months of age and without exception the children came from an environment that did not provide for the pasteurization of milk.

The most recent investigation in the United States of sufficient scope to provide significant data on the occurrence of tubercle bacilli of the bovine type in human pulmonary tuberculosis was reported by Beattie and Nicewonger (51) in 1942. A total of 366 strains of tubercle bacilli from the sputa of persons in sanatoriums and hospitals in various parts of California were studied. The strains were screened by cultural methods and those that were dysgonic or not typically eugonic were subjected to tests for virulence in rabbits. No strains considered to be bovine in type were found.

Earlier reports on the incidence of infection with bovine tubercle bacilli in human beings in the United States vary as follows. Of the 564 cases of tuberculosis reported by Park and Krumwiede (44) in 1910 the bovine type of infectious agent was present in 7.6 per cent. In Aronson and Whitney's (52) series and in the report by Van Es and Martin (53) the incidence of the bovine type of infection was 3.8 and 3.9 per cent respectively. In 1933 Chang (54) reported the results of a study he had made at a sanatorium in Massachusetts. His results indicated that in approximately a fourth of the 200 cases studied the infective organisms were of the bovine type. The figures of Chang are definitely unusual and probably do not represent a true indication of the extent of infection of human beings with the bacilli of bovine tuberculosis generally throughout the United States at the present time. As a matter of fact, it is generally believed that at present infection of human beings with the bacilli of bovine tuberculosis is of rare occurrence. Perhaps the subject should be investigated further by determining the type of tubercle bacilli present in the sputa of elderly persons who have been infected with

tubercle bacilli for perhaps two or more decades and who were *conceivably infected before the era of widespread tuberculin testing* of cattle and the pasteurization of milk

From the foregoing incomplete review of reports and investigations that have yielded information on the infectivity of bovine tubercle bacilli for human beings several pertinent facts become apparent (*1*) *Mycobacterium tuberculosis var bovis* is an important pathogen for human beings (2) A review of the literature by Price reveals that among approximately 18 000 cases of human tuberculosis in which the type of the infectious agent was determined the bacilli of bovine tuberculosis were responsible for the *infection in 10 per cent of the cases (3) The bovine type of infection* in human beings occurs most commonly in Great Britain with Denmark next in order of frequency (*4*) Cases of bovine tuberculous infections of human beings have a rather widespread geographic distribution although it must be emphasized that with the exception of the countries of Western Europe the problem has been insufficiently explored (5) The organism of bovine tuberculosis is capable of producing in human beings every form of tuberculosis of which the human type of organism is capable (*6*) Children are much more commonly infected by the bovine type of the tubercle bacillus than are adults The incidence of the bovine type of infection is highest among children less than five years of age * (*7*) The usual portal of entry of bovine tubercle bacilli in human beings is by way of the alimentary canal where the bacilli find their way through the medium of contaminated milk and other dairy products This probably accounts for the extrapulmonary situation of the vast majority of infections with bovine tubercle bacilli in man (*8*) While the extrapulmonary forms of tuberculosis predominate in the statistics dealing with human infection with the bacillus of bovine tuberculosis several hundred cases of genuine bovine pulmonary tuberculosis in man have now been established (9) According to Price lesions of extrapulmonary tuberculosis in a child in the absence of demonstrable tuberculosis in the parenchyma of the lungs or the tracheobronchial lymph nodes should be regarded as due to the bovine type of the infectious agent until proved otherwise (*10*)

* It is Rich s opinion that the difference in the frequency of infection in adults and in children due to the bovine tubercle bacillus can be explained on the basis of greater exposure of children to the infectious agent since milk constitutes a large part of the diet of children and the greater degree of natural resistance to tuberculosis possessed by adults

According to Griffith (13) the latent period of bovine pulmonary tuberculosis of alimentary origin may vary from less than one year to twenty six or more (*11*) The tuberculous dairy cow is a serious menace to human health and should not be tolerated by an informed society

Transmissibility Man to Bovine—Tuberculosis being a contagious disease it would be remarkable indeed if bovine tubercle bacilli could be passed successfully only from the natural host—the cow—to other cattle and to human beings Griffith and Munro (2) gave a brief account of an instance in which a herd was being tested repeatedly with tuberculin and the reactors were being eliminated Every new test revealed that some previously negative animal had become a reactor Although the source of the continuing infection was not suspected the herdsman was known to have been affected with pulmonary tuberculosis due to the bovine type of the organism and it is likely that the contagion in this case was from man to animal

Another example of the role of human beings in the transmission of bovine tuberculosis to previously noninfected cattle is the important observations reported in 1944 by Tice (55) of New York State In this instance in spite of repeated tuberculin tests the removal of all reactors and strict measures of sanitation infection continued to occur in new additions to the herd and it was not until three complete herds had been slaughtered on account of positive tuberculin reactions that the owner was suspected as the possible source of the infection Investigation revealed that the owner had been a patient at a tuberculosis sanatorium for a few weeks just prior to the first tuberculin test of the dairy herd Subsequent study of sputum from the owner of the dairy and of infected lymph nodes from cattle that had reacted to tuberculin revealed tubercle bacilli of the bovine type The evidence in Tice s report indicates definitely that the owner had contracted pulmonary tuberculosis from his original herd and had subsequently infected three new or replacement herds within a period of two and a half years Tice s observation emphasizes the importance of medical examination of human beings who may have access to the premises of a dairy in which repeated tuberculin tests reveal the presence of tuberculosis of obscure origin

A few cases have been reported in which human tubercle bacilli were demonstrated as the infective agents in naturally infected

cattle Feldman and Moses (56) reviewed the literature up to 1941 and reported a case of their own In many of the ten cases reported it was known that exposure to human beings suffering with pulmonary tuberculosis had occurred In most of the cases the infective process had remained localized in one or more lymph nodes of the bovine recipient although in one instance lesions occurred in the lung bronchial lymph nodes and in one of the mesenteric lymph nodes

It is obvious that persons who have active pulmonary tuberculosis should be excluded from premises frequented by cattle The possibility of transmitting the human type of tuberculous infection to cattle is rather remote but there is the greater possibility that as a consequence of infection with human tubercle bacilli cattle may be sensitized to tuberculin

Transmissibility Man to Man—Griffith and Munro also discussed the possibility of pulmonary tuberculosis of the bovine type being disseminated from one person to another The evidence in support of this happening if circumstances are auspicious is impressive Certainly the sputum of a patient who has pulmonary tuberculosis of the human type plays an important role in the spread of the disease from person to person and there is no reason for believing that sputum containing the bovine form of the tubercle bacillus would be less contagious From the point of view of virulence for human beings it is generally agreed by those who have had most experience with the subject that the bovine variety of the tubercle bacillus is not less virulent for human beings than are bacilli of the human type To quote Griffith and Munro It would be very surprising if these bacilli are not sometimes transmitted to healthy persons through the inspired air Cumming (57) presented evidence suggesting that air borne infection with the bovine type of tubercle bacilli does occur in dairy workers Griffith and Munro recounted instances in which strong presumptive evidence existed for the man to man transmission of the bovine type of infection

In 1939 Munro (58) reported a case in which it appeared likely that there had been transmission of the disease from father to child The child two and a half years of age had received no other than pasteurized milk and bovine tubercle bacilli had been cultured from the sputum of the father who was exceedingly careless in his personal habits and practiced no safeguards to avoid infecting his children Clinically the child gave evidence of tuberculosis of an

ankle joint and roentgenographically there were signs of minimal tuberculosis in the lungs Bovine tubercle bacilli were cultured from gastric contents obtained by lavage and from the urine of the child

Ruys (45) reported a case in which pulmonary tuberculosis was detected in a human being The tuberculosis was due to the bovine variety of the tubercle bacillus and it appeared that the infection had its source from a friend who had open pulmonary infection also due to bovine tubercle bacilli

Detection of Bovine Type of Infection in Human Beings—Since there are no recognizable clinical roentgenographic or pathologic features that provide reliable means whereby one can distinguish definitely human from bovine forms of tuberculous infection in man laboratory procedures are necessary for the precise diagnosis As was mentioned previously most mammalian strains of tubercle bacilli can be typed as bovine or human on the basis of certain cultural features of the two forms of the organism Most strains of the human type grow best in a medium containing glycerin but bovine strains on original isolation—with very few exceptions—prefer a nonglycerinated medium Furthermore most strains of the human type of the tubercle bacilli are eugonic and conversely strains of the bovine form of the organism are dysgonic in their growth propensities It must be kept in mind that the distinguishing features of various strains of tubercle bacilli based on the characters just mentioned constitute presumptive rather than unequivocal proof of the variety of tubercle bacillus under consideration To obtain convincing proof of the true character of a tuberculous infection it is necessary to inoculate at least guinea pigs and rabbits following the procedures mentioned previously (p 7) With the results of a properly conducted animal test available an investigator should be in a position to type or classify definitely the vast majority of strains of acid fast bacilli responsible for mammalian tuberculosis †

Various atypical strains of tubercle bacilli and instances of mixed infections with human and bovine types of tubercle bacilli are considered in the review articles by Price (42) and by Griffith and Munro (2)

† Griffith commented on certain features that should enable the experienced worker to recognize presumptively bovine tubercle bacilli present in sputum of man According to Griffith (08) if the bacilli in a stained film preparation of sputum are mostly short and uniformly stained and sometimes occur in small clumps the infective agent is almost invariably bovine in origin Griffith recognized the unreliability of such criteria for he stated Unfortunately one cannot rely upon morphology for the detection of cases of bovine pulmonary tuberculosis However such criteria may provide suggestive hint for additional studies of unusual strains of acid fast bacilli

Control of Infection from Cattle to Man.—As was mentioned previously, milk from tuberculous cows is frequently contaminated with tubercle bacilli. Butter, cream and cheese made from infected milk likewise contain the infecting organisms for varying periods. Even if the milk from tuberculous cows is not infected before it is excreted from the udder, there is always the possibility of the milk becoming infected from extraneous sources, of which manure in the dairy barn or in the barnyard is most important. Data assembled by Williams and Hoy (59) show definitely that dung from tuberculous cattle and even from cattle that were apparently healthy contained tubercle bacilli virulent for guinea pigs. The contamination of milk by barnyard filth occurs fairly commonly and should fecal material containing tubercle bacilli fall into the milk from the soiled surface of the udder and sides of the cow, the milk at once becomes dangerous to human health unless it is subjected to heat sufficient to kill tubercle bacilli.*

A sound and well proved method of safeguarding the public from the tuberculous dairy cow is the periodic tuberculin testing of all cattle and the slaughter of those animals that react positively to the test. As a further safeguard the proper pasteurization of milk intended for human consumption should be compulsory. Tonney, White and Danforth (61) compiled data on the occurrence of tubercle bacilli in market milk and found that of 16,700 samples of milk examined 8.66 per cent contained the infectious organism. The specimens were collected from several large centers of population and the studies were made by a large number of investigators working from 1893 to 1925. The incidence of contaminated milk varied from 2.7 per cent of specimens positive to 61.5 per cent positive. It should be pointed out that with a few exceptions the specimens of milk examined for tubercle bacilli in the studies compiled by Tonney, White and Danforth were obtained in European cities at a period when the danger of the bovine type of tubercle bacilli to human health was not generally recognized and as a consequence but little had been done to exclude tuberculous cows from the dairy herd. The data compiled by Tonney, White and Danforth, while not reflecting the present extent of contamination of milk by bovine tubercle bacilli in our American cities, do provide formidable evidence that milk, unless produced under the strictest sanitary and

* Maddock (60) showed that in some instances virulent bovine tubercle bacilli can survive a period of six months' exposure in soil, in soil and dung mixture and in dung.

regulatory control may not be a safe food for human consumption Pasteurization of milk at 145 F for thirty minutes renders tubercle bacilli nonviable In addition the thermal effect on many other milk borne infections that might initiate illness among consumers of the milk is an important attribute of the pasteurization process

With modern equipment pasteurization of milk is an economical and efficient procedure for rendering milk safe for human consumption without impairing to any measurable degree its value as a highly important and nutritious food For satisfactory results pasteurization plants should be operated under some public health authority and in strict conformity with regulations designed to provide maximal efficiency

Unless pasteurization is properly done a great deal of evil may result as a consequence of the safety that is implied if the phrase "pasteurized milk is used indiscriminately * Modern equipment proper supervision and frequent inspections are the essential factors for obtaining pasteurized milk that is safe and clean

The literature contains many reports of the efficacy of pasteurization in killing tubercle bacilli in cows milk However the reports of Price after a long experience with the situation in Toronto and the surrounding province of Ontario Canada should provide unequivocal evidence of the effectiveness of proper pasteurization in eliminating tubercle bacilli from the milk supply of a large city Relative to the situation at Toronto Price wrote as follows in 1939 Since 1916 when pasteurization was made compulsory there has not been a single proven case of bovine infection in the generation of children using city milk " This statement was based on the careful study of the etiologic factor in a series of 500 tuberculous children whom Price had investigated during a period of thirteen years She found that tubercle bacilli of the bovine type were responsible for 9 64 per cent of the extrapulmonary tuberculous infection It was of much significance that without exception children infected with the bovine type of the organism had their residence elsewhere than in the city of Toronto Price also established the fact that the children infected with bovine tubercle bacilli had consumed raw milk for some time or had always been fed raw milk

Further evidence of the ability of the pasteurization process to render bovine tubercle bacilli nonviable was obtained by Price by

* According to Buys (45) Boer found that inadequately pasteurized milk may contain living tubercle bacilli and hence provide to the consumer a false sense of security

subjecting to tests in guinea pigs 200 samples of pooled raw milk which were obtained from the pasteurization tanks prior to heating In 26 per cent of the samples the presence of virulent tubercle bacilli was demonstrated by the animal inoculation tests After heating the milk from which the previously mentioned samples were removed to 145°F for thirty minutes and cooling it quickly 100 additional samples were removed and used to inoculate guinea pigs None of the samples utilized in the second series of animal inoculations produced signs of tuberculosis in the recipients *

Another factor to be considered in the possible transmissibility of tuberculosis of animals to human beings is the infectivity of the musculature and other edible tissue of meat producing animals Tuberculosis in animals is ordinarily not a self limiting disease The infective agents are conveyed from an initial lesion to other situations of predilection by continuity by the lymphatics and by the blood stream If the disease is severe and of widespread distribution it is likely that at some phase of its progression the tubercle bacilli had a hematogenous spread and as a consequence all tissues are likely to have received a deposition of a few to many tubercle bacilli It is true that certain tissues such as the smooth and striated muscles have considerable intrinsic resistance to tuberculous infection and it is exceptional that a focus of the disease will develop and prosper in the musculature For this reason lesions of tuberculosis are found most frequently in the lymph nodes and parenchymal organs such as the lungs liver spleen mammary glands and testes

Apropos of tuberculosis of the musculature of cattle Day (62) recorded the incidence of the disease observed at the Branch Pathological Laboratory of the United States Department of Agriculture Chicago During a period of twenty three years a total of twenty five cases involving the voluntary muscles were encountered In fifteen of the cases the lesions were found among cattle slaughtered in Chicago Five of the animals were bulls two to six years of age three were steers two to three years of age two were heifers two years of age and fifteen were cows four to ten years of age In all

* The most reliable method for detecting tubercle bacilli in milk is by the inoculation of guinea pigs A 50 to 100 c c sample of the suspected milk is centrifuged for thirty minutes at 3 000 r p m The cream and the sediment are mixed the intervening fluid is discarded and the resultant material divided in two equal portions and used to inoculate two healthy guinea pigs subcutaneously Unless death occurs before the animals are killed for necropsy eight weeks after inoculation and examined for signs of tuberculosis

cases lesions of tuberculosis were found elsewhere in the respective carcasses and in fourteen of the twenty five cases the disease was generalized throughout the internal organs In view of the many millions of cattle carcasses examined by Federal meat inspectors in the slaughtering establishments in Chicago during the period when Days material was obtained the fact that only fifteen cases of tuberculosis involving the voluntary musculature were found is indicative of the rarity of this form of the disease

In the United States and many other countries a system of meat inspection is provided under either local or central governmental supervision to prevent the use by human beings of meat or meat products that are unwholesome The efficacy of such inspection depends on the competency of the inspecting personnel and the control that the inspecting authority exercises over the slaughtering establishment where the meat inspection is maintained

The meat inspection service administered by the United States Department of Agriculture is probably the finest in the world However Federally supervised meat inspection is required only for meat prepared for food by concerns engaged in interstate commerce and is not available for about 35 per cent of the nation s meat supply which is sold within the state in which it is prepared The latter is offered for sale either without the benefit of any inspection whatever or under city county or state inspection which is frequently inadequate owing to lack of trained personnel and the failure of public health authorities to insist that meat sold within the state should have as adequate inspection as that sold outside the state

In inspecting meat of tuberculous animals to determine wholesomeness for human consumption the Federal inspector is guided by regulations which are based on the principle that no meat shall be sold for food if it contains tubercle bacilli or if there is a reasonable possibility that it contains tubercle bacilli or if it is impregnated with the toxic substances of tuberculosis or associated septic infections Furthermore cognizance is taken of the fact that in most civilized countries meat is not eaten in the raw state and that the temperature necessary for cooking kills any tubercle bacilli that might conceivably be present * To be effective meat inspection should include both antemortem and postmortem examinations

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* For data pertaining to the presence of virulent tubercle bacilli in muscle heart blood spleen liver and lymph nodes of a variety of food animals affected with tuberculosis see report by Müller and Ishiwara (63)

TUBERCULOSIS IN MAMMALS OTHER THAN CATTLE

Dogs—Dogs are apparently equally susceptible to the bovine type and to the human type of tubercle bacillus The dog has a high resistance to the avian type of the tubercle bacillus and is exceedingly difficult to infect with this type even experimentally (10)



FIG 8—Multiple nodular lesions of tuberculosis of the lungs of an adult dog There was present also a large tuberculous mass in the wall of the terminal portion of the ileum Infection was due to the human type of the tubercle bacillus

Tuberculosis in dogs produces few symptoms that are characteristic and as a consequence the disease is seldom recognized while the affected animal is alive The etiologic agents capable of producing tuberculosis in dogs are also pathogenic for man The disease in dogs frequently affects the lungs where the lesions commonly un

dergo necrosis with extension of the bacilli laden cellular detritus to the larger respiratory channels Consequently the tuberculous dog is a potential danger to human beings and especially to children who frequently fondle and play with their canine pets in an intimate manner *

The exact incidence of tuberculosis in dogs is unknown This is especially true in the United States where only an occasional case has been reported Most of the figures relating to the incidence of tuberculosis in dogs are derived from the observations of investigators in Europe including Great Britain A compilation of 182 cases in which the bacillary type of the infecting agent was determined is shown in table 8

Table 8—Types of Tubercle Bacilli in 182 Cases of Naturally Acquired Tuberculosis in Dogs (Feldman and Code 65)

Geographic Area	Bacillary Type		
	Human	Bovine	Avian
England and Scotland	29	11	0
Continental Europe	103	32	1
Dutch East Indies	2	0	0
United States	3	1	0
Total	137	44	1

From the data presented in table 8 it is evident that the frequency of infection of dogs with the human type of the tubercle bacillus is about three times as great as the frequency of infection with the bovine type However this does not indicate that dogs are more resistant to the bovine than to the human type of infection The disparity in the incidence of the two types of the infecting agent in this series of cases can best be explained on the basis that there probably was a greater opportunity for exposure to infectious material containing tubercle bacilli of the human type Scott (64) investigated the probable source of exposure to 100 tuberculous dogs and found that fifty one had lived in restaurants or cafés where human sputum was at all times present on the floors and twenty eight had lived in intimate contact with sick persons

Some of the characteristics of tuberculosis in dogs may be summarized briefly as follows (1) The disease occurs most frequently in animals from one to five years of age (2) Symptoms while not

* For additional information on tuberculosis in dogs the following may be consulted Scott (64) Feldman and Code (65) and Lowell and White (66)

pathognomonic may include loss of weight cough and enlargement of the lymph nodes of the head and neck (3) The lungs and tracheobronchial lymph nodes are affected in about 60 per cent of the cases (figs 8 and 9) Other organs of predilection include the



FIG 9—Tuberculous nodule near the periphery of a lung of a dog (x70) Same case as shown in figure 8

liver and the kidneys The pleura pericardium and peritoneum are involved less frequently than the organs previously mentioned (4) The morbid anatomic changes may be those of caseous granulomatous nodules exudative tuberculous pneumonitis or circumscribed neoplastic like masses the last occur especially in the liver and kidneys Microscopically giant cells of the Langhans type frequently associated with tuberculosis in many other mammals do not occur (5) Acid fast bacillary forms are often numerous in preparations made from the caseous portions of the lesions

In the diagnosis of tuberculosis in dogs consideration should be given to (1) possibilities for infection as a consequence of contact with a human being who has *active pulmonary* tuberculosis or by the ingestion of contaminated cow s milk or tissue containing bovine tubercle bacilli (2) suggestive symptoms such as loss of weight and cough of variable duration and (3) the results of the tuberculin test

In conducting a tuberculin test on dogs 0 1 c c of a 1 100 dilution of tuberculin (OT or PPD) should be injected intracutaneously In animals in the terminal stages of the disease or those in poor general health due to mange or distemper the sensitivity to tuberculin may be suppressed

The public health aspect of tuberculosis in dogs, while only presumptive, is however worthy of consideration So far as is known no instance of transmission of the infection from an infected dog to a human being has been reported yet as mentioned previously the possibility of transmission from animal to man exists In tuberculous dogs having pulmonary lesions in which there is bronchiogenic spread or exudative tuberculous pneumonitis countless numbers of tubercle bacilli must find egress with the respiration and excretions and mix with the saliva Many of the organisms are undoubtedly swallowed and eliminated with the feces In severe destructive tuberculosis of the kidneys tuberculous bacilluria is probably fairly common These facts should be sufficient reasons for excluding tuberculosis in the diagnostic consideration of sick dogs in which the disease is suspected Obviously a tuberculous dog should be destroyed

Cats —Tuberculosis is an uncommon disease among cats especially in the United States Statistics from European sources indicate that the incidence of tuberculous infection among cats is about 2 per cent This figure will vary with different geographic locations and is largely dependent on the prevalence of tubercle bacilli in the milk supply Cats have a formidable resistance to infection with tubercle bacilli of the human and avian types but are susceptible to the bovine type of the organism * Available evidence indicates that in most instances the infection in cats has its portal of entry by way of the digestive tract This coincides with the fact that in districts where bovine tubercle bacilli occur in the milk tuberculosis also occurs among cats Milk containing bovine tubercle bacilli and consumed by cats is the obvious source of most infections in these animals

Information regarding the pathologic characteristics of natural tuberculous infections among cats was contributed by Dobson (68)

Kuwabara (67) attempted to infect a series of cats with human tubercle bacilli by inoculation by feeding and by exposing cats for two to three years in the homes of tuberculous patients In none of the animals did tuberculosis develop Progressive tuberculosis developed among all cats inoculated with bovine tubercle bacilli

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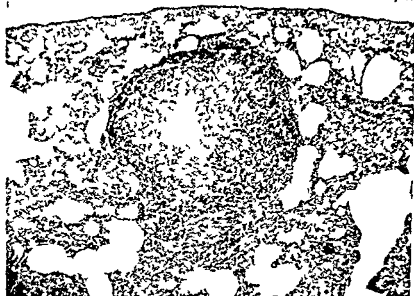


Fig 9—Tuberculous nodule near the periphery of a lung of a dog (x70) Same case as shown in figure 8

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pleural effusion in two tuberculous peritonitis and in one case there was a tuberculous nodule in the small intestine Dobson was unable to demonstrate acid fast bacilli in the saliva or the urine of the infected cats

The pathologic character of tuberculosis in cats is that of a disseminated miliary or nodular process that is commonly characterized by liquefaction (fig 10) Although the route of entry of the infective agent is through the mucosa of the intestine the intestine may be without demonstrable lesions In some instances severe tuberculous enteritis may occur but this would appear to be due to reinfection from the presence of tubercle bacilli in the ingesta as a consequence of an animal that has open pulmonary tuberculosis swallowing its own infective respiratory secretions It is likely that in the lungs the primary focus occurs subpleurally Extension of the process into the pleura and beyond may produce a purulent or fibrinous pleural reaction The pleura becomes greatly thickened and may eventually consist of a dense structure of fibrous connective tissue without distinguishing signs of tuberculosis

As the disease progresses in the lungs diffuse and striking pneumonitis may ensue As a consequence large regions of the lungs become solidified These eventually caseate or liquefy with the destruction of pulmonary tissue and the formation of cavities Entrance of tuberculous debris into the bronchioles may occur As a result bronchogenic spread of the infection is probably fairly common

Except in the early miliary form the tuberculous character of the lesions may not at once be recognized microscopically Giant cells of the Langhans type do not occur When caseation is present regions of caseation sometimes become calcified but this is uncommon Appropriately stained tissue may contain acid fast bacilli in sufficient numbers to be seen microscopically

The disease seems to have a special predilection for the lungs judging from the severity of the reaction in these organs In instances in which tuberculous pneumonitis is present large regions of the parenchymal tissue are distorted and destroyed beyond recognition

Generally speaking the pathologic character of naturally acquired tuberculosis among cats is similar in many respects to inoculation tuberculosis in the highly susceptible guinea pig The disease in both species is widely disseminated and highly destructive and

working at Edinburgh, Scotland Dobson observed the disease in eleven of a total of 505 cats examined In every instance the bovine type of the organism was the etiologic agent The sexes were about

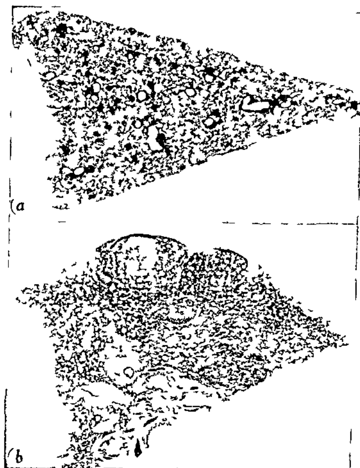


FIG 10—Pulmonary tuberculosis of the cat *a* Miliary type showing a moderate number of small discrete tuberculous foci (x4) *b* Nodular type showing large tuberculous nodules near the periphery The center of one nodule has undergone considerable caseation necrosis (x8) (Prepared from material kindly supplied by Dr J T Stamp Royal [Dick] Veterinary College University of Edinburgh)

equally represented The symptom most commonly observed was emaciation In Dobson s series the lesions occurred most frequently in the mesenteric lymph nodes lungs spleen kidneys and liver In three cases in Dobson s series open cutaneous lesions were present Tuberculous lymphadenitis also occurred in one instance there was

disease in swine has its origin in most instances from tuberculous chickens which are permitted the freedom of the farm premises and as a consequence deposit fecal material containing tubercle bacilli more or less promiscuously throughout the barnyard and hog lots In addition garbage fed to swine fairly frequently contains uncooked viscera of tuberculous chickens which have been dressed for human consumption

Table 3 —The Number of Swine Slaughtered under Federal Supervision Showing the Percentage in Which Lesions of Tuberculosis Were Found and the Percentages of the Total Number Killed in Different Years that Were Condemned or Sterilized

Year	Number	Percentage Tuberculous	Percentage Condemned or Sterilized
1917	40 210 847	9 89	0 41
1922	39 416 439	14 30	0 39
1927	42 650 443	13 54	0 31
1932	45 852 422	11 38	0 18
1937	36 226 309	9 48	0 08
1942	50 133 871	7 96	0 054
1943	56 867 080	7 08	0 046
1944	74 946 117	6 91	0 042
1945	49 468 458	7 19	0 046

Data supplied through the courtesy of Dr A E Wight Tuberculosis Eradication Division United States Department of Agriculture

Tuberculosis of swine due to the human type of infection probably occurs rather infrequently although precise information regarding this is not available In a study on the type of tubercle bacilli responsible for tuberculous lesions in garbage fed hogs it was shown that among 264 animals examined after slaughter 28 4 per cent had tuberculosis Subsequent studies to determine the type of the infecting organisms in each of the diseased carcasses showed that 74 5 per cent of the bacterial strains were of the avian type and 25 5 per cent were of the human type (71)

Generally speaking the bovine type of the tubercle bacillus is capable of producing in swine a more severe and more widely disseminated tuberculosis than either of the other two forms of the organism However it has been shown that although avian tuberculosis in swine is predominantly a localized disease of the lymph nodes the disease may become widely distributed with involvement of the liver spleen lungs and kidneys (72) (fig 11) When infected perorally swine are less susceptible to the bacilli of human tuberculosis than to either of the other two types Natural infection of swine

there are many similarities in the microscopic appearance of the lesions in the various organs

In spite of the absence of known instances in which tuberculous infection of cats has been communicated to human beings one can not ignore the possibility of this occurring The tuberculous cat like the tuberculous dog must be considered as a potential source of tuberculous infection to man and particularly to children Especially likely as a source of infection to man would be open cutaneous lesions the discharge from which contains numerous tubercle bacilli

Swine —The susceptibility of swine to *Mycobacterium tuberculosis* is unique in that this animal is susceptible although to variable degrees to each of the three common types of tubercle bacilli responsible for tuberculosis in warm blooded animals † Because of this fact the incidence of tuberculosis in this common domestic animal provides an index to the amount of tuberculosis in cattle man and chickens in a given community It must be recognized however that the preceding statement is subject to at least one reservation in that the possibility for exposure constitutes an important factor in the relative incidence of infection by the respective bacillary types of the organism

A fairly satisfactory concept of the incidence of tuberculosis in swine in the United States during the past twenty eight years may be obtained by referring to table 9

The incidence of infections due to each of the respective bacillary types of the tubercle bacilli among the tuberculous animals represented in table 9 is not known However observations by Van Es and Martin (70) showed that in tuberculous swine from Nebraska the avian tubercle bacillus was responsible for more than 88 per cent of the infections Furthermore while the bovine type of infection in swine has steadily declined as tuberculosis has been eliminated from cattle the total percentage of tuberculosis in swine has continued at a relatively high level The impression at the present time which has been supported by experimental evidence is that in the United States tuberculosis of swine is caused in the vast majority of instances by the organism of avian tuberculosis ‡ The

* Additional information regarding tuberculosis in cats will be found in the report by Lovell and White (69)

† Information regarding susceptibility of swine to the vole bacillus is not available

‡ A detailed account of avian tuberculosis in swine will be found in the monograph by Feldman (10)

human and avian forms of the organism Although only a few cases have been reported of horses being infected naturally with avian tubercle bacilli severe and fatal infection can be accomplished experimentally by the intravenous injection of fully virulent bacilli of the avian type (10)

In America tuberculosis has been but rarely observed in the horse most of the cases reported have been of European origin Even in Europe the evidence fails to indicate that tuberculosis in horses is of common occurrence Indicative of the infrequency of equine tuberculosis are figures from German sources (10) In the period from 1904 to 1924 the incidence of tuberculosis in cattle was 18 98 per cent in swine 2 10 per cent in goats 0 85 per cent in sheep 0 16 per cent and in horses 0 14 per cent

The cases reported indicated definitely that bovine tubercle bacilli are responsible for the great majority of tuberculous infections in horses In a series of fifty five cases reported by Griffith (73) from England bovine tubercle bacilli were obtained in all except two In one of the latter the causative agent was the human type of the tubercle bacillus and in the other avian tubercle bacilli were identified

Since the bovine tubercle bacillus is the organism mainly responsible for tuberculosis in horses it is evident that the occurrence of the disease in the horse is largely dependent on the occurrence of tuberculosis in cattle The extremely low incidence of tuberculosis in cattle in the United States provides adequate explanation for the paucity of the disease in horses in this country

Although a horse affected with the bovine type of tuberculosis with involvement of the lungs and kidneys could become a hazard to human health the possibility of horses in the United States becoming infected is so slight as to make equine tuberculosis of no significance to public health However the possibility of the transmission of the bovine type of infection in the horse to previously noninfected cattle maintained on the same premises is worthy of consideration in situations where the source of infection in cattle cannot be explained

Sheep and Goats—Tuberculosis is extremely rare in sheep According to Feldman (10) among 147 000 000 sheep slaughtered in abattoirs under Federal supervision from 1928 to 1936 tuberculosis was recognized in less than fifty In European countries the disease is likewise seldom encountered

with human tubercle bacilli seldom results in more than localized tuberculous adenitis The lymph nodes of predilection are the mesenteric the submaxillary and the cervical

Swine affected with human or bovine tubercle bacilli are not necessarily a serious hazard to human health provided the carcasses of such animals are subjected to a proper postmortem examination by a qualified meat inspection service It must be recognized however that lesions of tuberculosis in swine due to the bovine or to the

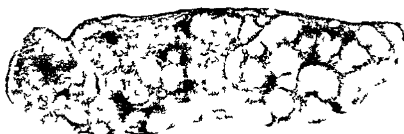


FIG 11 —Numerous nodular lesions of tuberculosis of the spleen of a swine Infection in this instance was due to the avian type of the tubercle bacillus

human type of the tubercle bacillus constitute a possible occupational hazard for slaughterhouse employees and meat inspectors Meat inspectors especially are likely to come in contact with infectious material since handling of diseased viscera and lymph nodes with the bare hands is a routine procedure Manipulation of diseased tissues cannot be avoided and the possibility for cutaneous infection exists

When infection of swine by human tubercle bacilli is known the fact should be of interest to those concerned with the public health If the dissemination of human tubercle bacilli is occurring in a community in sufficient numbers to produce tuberculous lesions in swine, it is reasonable to believe that the source of such pathogens is a potential danger to human beings

The public health aspect of the avian type of tuberculous infection in swine is probably negligible since as will be pointed out later human beings appear to be highly resistant to this type of the tubercle bacillus

Horses —Horses have a low to moderate susceptibility to the bovine type of the tubercle bacillus but are relatively resistant to the

in chickens is characterized by its insidious course its chronicity the presence within the lesions of exceedingly large numbers of the infectious bacteria and ulcerative lesions of the intestine which provide a favorable circumstance for a gross dissemination of the infectious agent mixed with the fecal material

The infection is acquired in most instances by the infective agent entering the digestive tract with food or water although infection by the respiratory tract has been reported Lesions occur most frequently in the intestines the spleen liver lungs and bone marrow Occasionally cutaneous lesions have been observed

The pathologic character of the disease in chickens is that of discrete granulomatous nodules of variable sizes A few to many nodules may occur along the intestines and firm yellowish elevated foci are present usually in the spleen and liver (fig 12) In some cases the progression of the infection in the spleen or liver is so great and so rapid that rupture of the organ takes place as a consequence of the hypertrophy When this happens fatal hemorrhage usually ensues

Tuberculous chickens are likely to be thin or even emaciated The disease can be detected best in the living bird by the tuberculin test using avian tuberculin although chickens in the later stages of the disease may fail to react to tuberculin The appearance at necropsy of the lesions of tuberculosis in chickens leaves no doubt as to the nature of the disease The appearance of the lesions is characteristic

The disease can be controlled by denying the birds the freedom of the farm premises and by the application of hygienic measures in poultry husbandry A tuberculosis free flock of young chickens confined to clean and noncontaminated enclosures will probably remain free from tuberculosis The yearly addition of young though noninfected chickens to a previously established flock where tuberculosis exists and where the birds range unrestricted throughout the barnyard will insure the perpetuation of the disease

Where tuberculous chickens exist there is abundant opportunity for the infection to spread to other chickens and to susceptible heterologous hosts As mentioned previously the fecal material abounds in tubercle bacilli which have a considerable ability to remain viable outside the body of the host for a long time It is known that the organism of avian tuberculosis will remain viable and pathogenic in the litter and soil of an infected barnyard for several years after the premises have been contaminated

Sheep are known to be susceptible to both the avian and bovine types of tubercle bacilli While natural infection due to the human type of the organism has been reported it is generally believed that sheep are fairly resistant to the bacillus of human tuberculosis

On the basis of limited statistics acquired tuberculosis in goats appears to be extremely infrequent Among approximately 317 000 goats examined at necropsy by the Federal Meat Inspection Service only one case of tuberculosis was encountered However the fact that goats are highly susceptible to the bacillus of bovine tuberculosis is sufficient reason for not considering too lightly the part that goats may play in the transmission of the bovine type of tuberculous infection to man If associated with tuberculous cattle goats are likely to contract tuberculosis Golden is quoted by Myers (25) as having demonstrated six tuberculous goats in a herd of forty two The bacillary type of the infectious agent was not mentioned but it is reasonable to assume that it was bovine The fact that goats are susceptible to the bovine type of the infective agent should make it obvious that goats used for the production of milk for human use should be subjected to the tuberculin test As a further safeguard Myers recommended that goats milk should always be pasteurized if it is to be used for human consumption

The reported cases of naturally acquired tuberculosis in goats have been due in most instances to the bovine type of the organism The avian type of infection has been identified in a few cases The goat has a marked resistance to the human type of tubercle bacillus

TUBERCULOSIS OF CHICKENS

Tuberculosis of chickens is widely distributed throughout most of the northern hemisphere and is one of the most common and in some areas one of the most serious diseases affecting the domestic chicken The disease is particularly prevalent in the North Central portion of the United States where in some districts 60 to 70 per cent of the flocks are affected

Chickens are susceptible only to the avian type of the tubercle bacillus However the organism of avian tuberculosis is virulent in varying degrees for several heterologous hosts including certain mammals such as swine and to a lesser degree cattle † The disease

For a comprehensive account of tuberculosis in chickens see the monograph by Feldman (10)

† A review of the pertinent information regarding the pathogenicity of avian tubercle bacilli for cattle may be found in the monograph by Feldman (10)

AVIAN TUBERCULOSIS IN MAN

One of the most important yet most confusing questions concerning tuberculosis in chickens is whether or not the infection is communicable to human beings The question has been the subject of much speculation and a careful review of the literature reveals that many indeed of the cases of alleged avian tuberculous infections in man have been either inadequately described or incompletely or incorrectly studied As a consequence the reviewer must if he is critical come to the conclusion that infection of human beings with the avian type of the tubercle bacillus has not in most instances been proved by acceptable evidence Feldman (10) reviewed the cases reported up to 1938 and concluded that in the majority a diagnosis of avian tubercle bacillus infections was questionable or erroneous Rich (5) analyzed the data presented up to 1944 and concluded that if progressive tuberculosis is ever produced in the human being by the avian bacillus it must be only very rarely

In spite of the skepticism that logically follows a critical examination of the evidence presented to support most of the reported cases of alleged avian tubercle bacilli infections in man it must be admitted that in a few cases at least avian tubercle bacilli have been demonstrated from morbid materials derived from human beings However while the possibility of infection of man by the organism of chicken tuberculosis must be recognized it is also true that the pathogenicity of this type of the tubercle bacillus for the vast majority of human beings is practically nil That an occasional infection in man may and probably does occur seems to be true but in comparison with the virulence of the human and bovine types of the tubercle bacillus for man information available at the present time indicates that the avian type is practically without significance

Investigators should not however consider the question settled and should subject suspected material to procedures that will elicit results that can be interpreted with confidence The extreme rarity of infections of human beings with avian tubercle bacilli and the skepticism of many who doubt that such infection ever occurs make it exceedingly important that every alleged case be firmly established by convincing data To establish the bacillary type of some

The question of the possible relation of Hodgkin s disease to avian tuberculous infection has been discussed by Feldman (10) and by Rich (5)

The question whether eggs laid by tuberculous birds contain avian tubercle bacilli has been the subject of considerable investigation * The accumulated evidence indicates that occasionally avian tubercle bacilli are present in eggs from tuberculous hens This does not occur often—probably in less than 1 per cent of the eggs laid by infected chickens



FIG 12—Naturally acquired tuberculosis of the abdominal viscera of an adult chicken *A* *Nodular intestinal lesions* *B* *Liver* *C* *Spleen*

Assuming that a small percentage of eggs from tuberculous hens contain virulent tubercle bacilli and accepting the fact that most of the eggs from chickens are consumed by human beings it is important to know the temperature necessary to render the bacilli non viable The temperature necessary to obtain an egg that is soft boiled is not sufficient to kill the bacteria some survive in the zone between the soft and firm portions of the egg Time and temperature sufficient to obtain eggs that are hard boiled are ordinarly sufficient to kill avian tubercle bacilli that may be present However there is some evidence to indicate that the time of boiling must be extended to ten minutes to insure the desired results

* For a detailed consideration of the question of eggs containing avian tubercle bacilli see the review by Feldman (10)

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strains of *Mycobacterium tuberculosis* is not a simple matter and *frequently extensive studies are necessary to determine definitely* that a given strain is or is not one of the commonly accepted types While several factors are of importance in the type identification of tubercle bacilli the most convincing evidence is obtained from properly conducted tests of pathogenicity (Procedures for the determination of types of tubercle bacilli are given on page 6) *

ITEMS OF NOTE

1 While it is generally recognized that there exist three bacillary types of tuberculous infection the ability of each of the three types to produce progressive tuberculosis in certain heterologous hosts is not well appreciated If this fact is fully understood and its importance completely realized the necessity of a comprehensive plan of control and eradication of tuberculosis becomes evident Ideally the goal should be the elimination of tuberculous infections from all species

2 From a public health point of view tuberculous cattle constitute the most important animal source for tubercle bacilli that are virulent for man In the United States bovine tuberculosis has been reduced to a very satisfactory level yet so long as a single focus of infection remains there exist the essentials necessary for the dissemination of the infection The attack against the tubercle bacillus must be prosecuted with vigor and without compromise An attitude of complacency or one in which satisfaction with past achievements takes precedence over the importance of the task yet to be done will defeat any plan of approach no matter how adequate it may appear to be

3 Finally it is appropriate to emphasize that the remarkable achievement of the veterinary profession in practically eliminating tuberculosis from cattle in the United States constitutes a notable example for the guidance of physicians who are concerned with eliminating tuberculosis from human beings The problem must be attacked nationally and with vigor with the thought ever in mind that *tuberculosis is a highly contagious disease Those who have the disease in the contagious phase must be segregated from those who are not infected*

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* Requirements for a diagnosis of avian tuberculous infections in man are outlined also by Rich (5)

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CHAPTER II

ANTHRAX*

Anthrax is primarily a disease of animals secondarily man is infected from an animal either by direct or indirect means Other designations for the disease which have been used are malignant pustule splenic fever charbon murrain and wool sorters disease

HISTORY

The origin of anthrax is lost in antiquity About 1491 B C Moses is quoted as threatening Pharoah with an epidemic among his horses cattle and sheep as follows

Behold the hand of the Lord is upon thy cattle which is in the field upon the horses upon the asses upon the camels upon the oxen and upon the sheep there shall be a grievous murrain" (1)

The disease is considered by many authors to have been anthrax The severity of the outbreak is indicated by the statement that all the cattle of Egypt died

Classical writers in the centuries that followed alluded to outbreaks among animals that in all probability were anthrax Homer mentions it Virgil describes it quite accurately in epidemic form in animals Hippocrates Galen and Pliny describe carbuncles which are considered anthrax by modern authorities Numerous writers during the medieval ages mention devastating epidemics of the disease in animals Not until near the end of the sixteenth century however was it suspected that the disease was transmissible to man In 1613 in the south of Europe it developed into a scourge which carried off 60 000 people In ancient Anglo Saxon records there appear accounts of recipes charms and incantations for the cure or prevention of 'black bain as anthrax was then called

The beginning of scientific literature on anthrax is marked by the publication of Charbon Malin by Fournier in Dijon France in

* Prepared by Henry Field Smyth M D Dr P H

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1769 The Academy of Dijon offered a prize essay on the subject which resulted in some remarkably accurate descriptions of the dis ease in man and animals Chabert (2) in 1780 distinguished dif ferent forms of anthrax in man from other septic conditions of the skin and Barthelemy in 1823 proved the contagious nature of the disease in animals

The cause of anthrax at this time was a moot point, theories being bound up in all the hazy and illogical notions of the pre Pasteur period Delafond (3) a French veterinarian held that anthrax in sheep was caused by an excess of blood circulating in the vessels due to too copious and substantial feeding Heusinger (4) was of the opinion that anthrax in man was due to a malarial neurosis de pendent upon various conditions of the soil and climate Other ideas included the influence of soil summer heat storms, insanitary con ditions of the stables and the like

Among such a confusion of ideas with anthrax killing off from 25 to 50 per cent of the flocks of sheep and so prevalent in France and other European countries that farming was almost at a standstill (5) a period of observation and investigation began about 1850 which culminated in the identification of the anthrax bacillus by Koch in 1876 (6) and the production of a preventive vaccine by Pasteur in 1880 (59)

Historically anthrax has a double significance It was the first dis ease of man and animals shown to be caused by a micro organism *and the first disease against which a bacterial vaccine was found to* be effective

THE ETIOLOGIC AGENT

Anthrax bacilli in the blood were first seen by Pollender (7) in 1849 His description was not published until 1855 however and meanwhile Davaine and also Rayer (8) had called attention to these peculiar bodies about twice the size of a red blood corpuscle which were present *in the blood of infected animals Brauell (9) in 1857* and Delafond in 1860 (3) both observed the same organisms but none of the investigators up to this time realized their full signifi cance The researches of Pasteur into the field of what was destined to become the science of bacteriology stimulated Davaine (10) again to take up the study of these organisms In 1863 he demon strated that only the blood of animals sick with the disease con tained the organism (10) and in 1873 he showed that when this

blood was passed through a clay filter it was harmless for other animals (10) In 1876 Robert Koch (6) cleared up the whole matter by cultivating the organisms outside the body in pure culture and again producing the disease

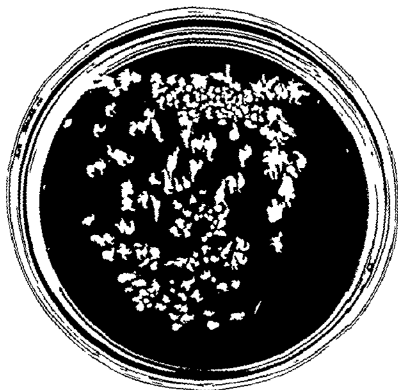


FIG 18 —Anthrax colonies natural size on surface of plain agar plate *twenty four hour growth made direct from suspension in saline solution* of blood from case of anthrax in cattle Note irregular shape of colonies many with tails (comet shaped) (From Stein C D Vet Med 1943 38 130–139)

Bacillus anthracis is one of the largest organisms among the pathogenic *bacteria measuring from 1 to 1 25 microns in thickness and 5* to 10 microns in length It has the further distinction of being one of the most resistant of organisms among the pathogens In its spore stage it has been found to survive in a dried condition for many years (11) Graham Smith (12) testing anthrax spore survival found that with dried spores exposed to diffuse sunlight at room tempera ture 50 per cent were incapable of germination after a few months

a considerable portion of the remainder germinated after 10 years but all seemed to be dead in 23 years Chemical disinfectants are not very effective against the spores except in strong solutions or over long periods of time—liquor cresolis compositus 5 per cent seven hours carbolic acid 5 per cent two days mercury bichloride 10 per cent twenty minutes, and formalin 10 to 20 per cent ten

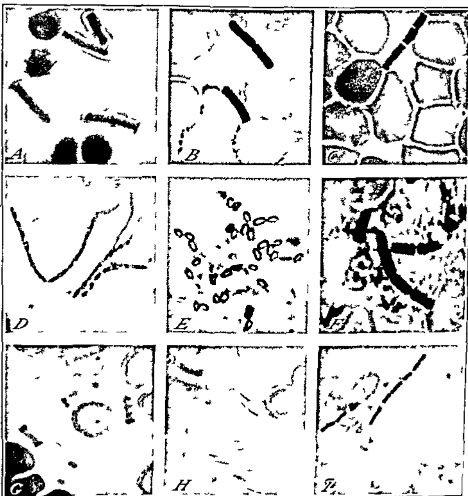


Fig 14—Stained anthrax bacilli and spores *A* bacilli in sheep blood (methylene blue) × 1 700 *B* bacilli in guinea pig blood (Giemsa's stain) × 1 600 *C* bacilli in guinea pig blood (Hastings stain) × 1 600 *D* sporulating organisms from spleen (from case of anthrax in cattle) × 1 400 *E* anthrax spores from culture × 1 900 *F* bacilli in blood stained with methylene blue (photograph taken with polarized light) × 2 000 *G* and *H* so-called shadow or ghost forms × 1 500 *I* bacilli from spleen of guinea pig (note long chains) × 1 400 (From Stein C D Vet Med 1943 38 130–139)

minutes Iodine 0 5 to 1 per cent will sterilize skins in two hours or less (13) In dry air the organisms are destroyed at 200°F in 24 hours (14) The vegetative forms free from spores, are easily destroyed by the usual methods of disinfection

In culturing other less resistant types of bacteria will overgrow *Bacillus anthracis* but when these have been destroyed by the correct degree of heat, it is easily cultivated on all ordinary nutrient

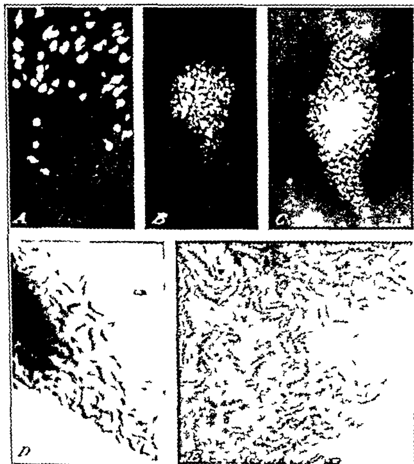


FIG 15—Anthrax colonies on surface of plain agar plates eighteen hour growth made direct from suspension in saline solution of spleen swab from case of anthrax in cattle A small and medium irregular shaped colonies natural size B small colony (note ground glass appearance) × 10 C large comet shaped colony (note ground glass appearance) × 10 D portion of colony C showing border × 30 E border of colony C × 100 (From Stein C D Vet Med 1943 38 130–139)

media forming characteristic colonies which are not difficult to identify These colonies have a ground glass or medusa head appearance curled with marginal filaments always returning to the colony and not showing free ends In filaments of a 24 hour culture cell divisions are not easily seen when examined under the oil immersion lens through a cover glass Spores do not develop until after 24 hours on standard agar As with several other pathogens two types of colonies have been noted rough and smooth the rough or R type being more virulent After the use of some antiseptics R" colonies may disappear and only the S type remain coincident with loss of virulence

It has recently been shown that there is a definite antagonism between the anthrax organism and the colon bacillus (15) When allowed to grow in mixed culture the anthrax organisms not only decrease in relative number but also in virulence A similar antagonism has been shown between anthrax and *Pseudomonas aerugenosa* and also one of the mycoides group of organisms

While generally referred to as an aerobic organism the anthrax bacillus can be grown anaerobically under which condition it has a somewhat altered morphology produces no spores and is less virulent (16) This corresponds somewhat with its behavior in man as it is a non spore former in the body forming spores only when having an abundant supply of oxygen This fact is the basis of the regulation as to the disposal of anthrax infested carcasses mentioned later

GEOGRAPHIC PREVALENCE

Anthrax occurs in all parts of the world In certain European countries where restrictive measures have been enforced together with preventive vaccination as in England France and Germany the disease in animals is now rather infrequent In other parts of the world especially the Asiatic countries of Siberia Persia Tibet China India and Arabia where sanitary science has not been developed anthrax in animals is very prevalent It occurs in many parts of South America Africa and Australia Legge (17) lists as countries most likely to supply infected materials such as wool hair hides and skins China India Central Asia Straits Settlements Persia Mesopotamia Asia Minor Japan Russia Egypt and Africa American experience would add South America and Mexico to this list

Questionnaires sent out in the spring of 1939 by Smyth have thus far shown that Great Britain Germany France Poland Belgium

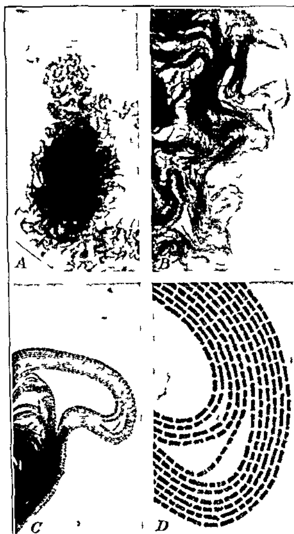


FIG 16 —Photomicrographs of an anthrax colony removed from surface of plain agar plates by impression method fixed mounted and stained with methylene blue *A* colony from anthrax field strain (× 45) *B* border of the same colony (× 145) *C* extreme margin of a portion of the border shown in *B* Note the wavy hairlike parallel arrangement of bacterial filaments composing upper and lower loops (× 400) *D* upper loop shown in *C* highly magnified to show arrangement of individual bacteria composing the long chains (× 1 600) (From Stein C D Vet Med 1943 38 130–139)

Italy Norway, Denmark Sweden Esthonia Finland Australia Philippine Islands India Turkey, Siam Java Sumatra Union of South Africa Rhodesia, Celebes Moluccas, Iraq Belgian Congo Guatemala Puerto Rico and Hawaii have animal anthrax more or less prevalent

In the previous five years New Zealand had had no animal or human cases, Borneo none Liberia four cases in animals but none in man and the Netherlands three cases in man but none in animals

The outlook however, becomes somewhat more hopeful for the future when it is considered that preventive inoculation of livestock is being practiced to some degree in 23 of the 27 countries mentioned above This measure is being used very extensively in the United States but as yet we continue to have many outbreaks of animal anthrax and human anthrax arising from the handling of domestic materials is not uncommon

Anthrax occurred in North America quite early in the days of the colonies Carpenter (18) traced the infection in Louisiana back to the time of its settlement by the French It was believed to have been prevalent among the deer of that region The cattle were likewise attacked annually so that by 1835 it existed in all parts of the state Carpenter states however that it seems not to have been even noticed in the medical annals of America " In 1835 he reported a large number of human cases Later references in that state as well as other lower Mississippi and Gulf States in the years that followed indicate that anthrax was more or less endemic in that region (19) The first human case in the United States of which there is record occurred in Philadelphia in 1834 (20) Murrain or anthrax was at that time prevalent among cattle fed on the common Several persons who skinned such animals developed lesions on the hands

In New England Osborn (21) could find no mention of anthrax in the colonial records of Massachusetts In 1852 a report appeared by a physician in Salem who had seen six different cases in previous years (19) From 1853 to 1869 at Walpole Massachusetts 26 cases occurred traceable to a hair factory (21)

Numerous references have appeared since that time in medical literature indicating that anthrax has existed especially in the northern states of the Atlantic seaboard in California and in the Central Gulf States In Louisiana in 1924 20 000 head of cattle perished from the disease in 43 out of 64 parishes (22)

Animal anthrax tends to appear in river valleys Stein (23) states that it is prevalent in southeastern South Dakota northeastern Nebraska the Texas Gulf coast the delta region of the lower Mississippi and in the Mississippi valley in Arkansas Mississippi and Louisiana in all of which areas widespread outbreaks occur from time to time Streams are often contaminated with surface drainage from anthrax soil and may carry the infection to distant points especially during floods and overflows The outbreaks usually occur when livestock are in pasture and tend to follow hot dry summers in which normally swampy areas are dried up and the regular growth of herbage becomes scanty necessitating grazing close to the soil

Smyth as Chairman of the Committee on Anthrax of the Industrial Hygiene Section of the American Public Health Association has been reporting anthrax incidence in the United States since 1919 and in October 1939 presented a 20 year summary 1919-38 (24) In the first five year period 1919 23 only 15 states reported human cases but further information since obtained added 10 to this list In 1924 28 27 states reported human cases 1929-33 35 states and 1934-38 37 states all of the states replying to the questionnaire for the first time

In October 1944 a further detailed report for the 1939 1943 period (24) added Alabama and the District of Columbia for the first time to areas reporting human cases At some time during the twenty five year period every state except Idaho and South Carolina has reported one or more human cases In the 1939 1943 period 29 states reported 408 human cases Of these 316 cases were of industrial origin (from hides and skins wool and hair) and all but two of these occurred in the six states of Delaware Massachusetts New Hampshire New Jersey New York and Pennsylvania

From table 10 which shows the geographic distribution of animal and human anthrax in the United States it may be seen that with the possible exception of Idaho there is not a state in which either animal or human anthrax has not been recognized in the twenty five year period preceding 1944 In each succeeding five year period new states which had not previously reported human cases of agricultural origin have so reported until now at least three quarters of the states have so reported so that although the larger number of human cases are of industrial origin they are concentrated in a few states and are quickly recognized and promptly

Table 10 —GEOGRAPHICAL DISTRIBUTION OF ANTHRAX IN THE UNITED STATES 1919 1943

State	Animal Anthrax Occurring		Human Anthrax Occurring		Comments
	Before 1939	1939–1943	Before 1939	1939–1943	
Alabama	+	+	−	+	
Arizona	−	−	+	+	
Arkansas	+	+	+	+	
California	+	+	+	+	
Colorado	+	+	+	+	
Connecticut	+	−	+	−	
Delaware	+	?	+	+	No animal anthrax in 1942 or 1943. Human cases chiefly industrial
D C	−	−	−	+	Probable source hairbrush
Florida	+	−	+	−	
Georgia	+	+	+	+	
Idaho	−	−	−	?	Diagnosis disputed
Illinois	+	+	+	+	
Indiana	+	−	+	−	
Iowa	+	+	+	+	
Kansas	+	−	+	−	
Kentucky	?	?	+	−	No reports received re animal cases
Louisiana	+	+	+	+	
Maine	+	−	+	+	
Maryland	+	+	+	−	
Massachusetts	+	+	+	+	Human cases chiefly industrial
Michigan	−	−	+	−	
Minnesota	+	+	+	−	
Mississippi	+	+	+	+	
Missouri	+	+	+	+	
Montana	+	+	+	?	Diagnosis disputed
Nebraska	+	+	+	?	Doubt completeness of reporting human cases animal anthrax prevalent
Nevada	+	+	+	−	
New Hampshire	+	−	+	+	Human cases chiefly industrial
New Jersey	+	+	+	+	Human cases chiefly industrial
New Mexico	?	?	+	+	No reports received re animal cases
New York	+	+	+	+	Human cases chiefly industrial
N Carolina	+	+	+	+	
N Dakota	+	+	+	+	
Ohio	+	−	+	+	
Oklahoma	+	−	+	+	
Oregon	+	+	+	+	
Pennsylvania	+	+	+	+	Human cases chiefly industrial
Rhode Island	?	?	+	−	No reports received re animal cases
S Carolina	+	−	−	−	
S Dakota	+	+	+	+	
Tennessee	?	?	+	?	Human case diagnosis disputed No animal cases 1941–43 previous records destroyed
Texas	+	+	+	+	
Utah	+	+	+	+	
Vermont	+	−	+	+	
Virginia	?	?	+	−	No reports received re animal cases
Washington	+	−	+	−	
West Virginia	+	−	+	+	
Wisconsin	+	+	+	+	
Wyoming	+	−	+	−	

treated while the more serious problem lies in the widely scattered cases of agricultural origin

THE DISEASE IN ANIMALS

Practically all animals domestic and wild are subject to anthrax to a greater or less degree Sheep and cattle are the chief sufferers but other domestic animals such as horses goats and even hogs may contract the disease on occasion Dogs have been known to become infected through eating the carcasses of animals dead of the disease Fowls are practically immune except under adverse conditions such as those in Pasteur s classical experiment where the body tempera ture was lowered several degrees by partial immersion of the bird in cold water In his 1939 report (24) Smyth refers to anthrax con tracted from minks in commercial minkeries where anthrax infested horsemeat had been fed to the animals and a report from Siam re fers to anthrax in elephants The small laboratory animals such as guinea pigs mice and rabbits die very quickly after inoculation

Infection of animals ordinarily takes place by ingestion of the or ganism rather than by contact Pastures in which infected cattle have roamed may remain contaminated for years and prove fatal to any stock turned thereon to graze Pastures contaminated by tan nery wastes have been described by Eichhorn (25) and by others as a menace to cattle as are streams into which tannery wastes are discharged and from which cattle or other animals may drink Anthrax organisms may be carried from place to place by birds and small animals They have been found on the beaks and feet of buzzards which have fed on animals dead of the disease The dog cat opossum and chicken all may harbor live spores in the feces after eating infected flesh and thus serve as dangerous carriers in spreading the contagion to new territory Morris (26) cites a case in which it was claimed that virulent pores were found in the feces of a dog eight years later Infection by ingestion may occur from eating hay forage or other crops which have been grown on in fected pasture land or otherwise contaminated with anthrax spores Smyth (24) reports a small epidemic in cattle in Maryland due to feeding infected blood meal Ten Hoopen (27) states that the ma jority of cases of anthrax among Dutch cattle are traceable to im ported infected fodder As stated in Smyth s 1934 report 80 per cent of cases reported in Great Britain arise on premises upon which the disease has not existed within the previous five years The use

of artificial feedstuffs appears with great frequency in association with such outbreaks bone meal seeming to have been the source of infection in several instances Kelland (28) suggests that the use of imported feed in 248 out of 395 anthrax outbreaks in animals in England and the simultaneous use of imported feed and artificial manure in 40 more, may be significant

Biting flies may be a factor in the spread of anthrax not only from animal to animal but also from animal to man Anthrax spores have been found to remain alive in flies for 20 days being found in the feces Infection through abrasions cuts and scratches can likewise spread the disease but such factors are of small importance in animals compared to ingestion

The disease in animals may appear in three forms—apoplectic acute or subacute Washburn (29) describes these different conditions as follows

"The apoplectic form is most frequently seen attacking cattle or sheep at the beginning of an outbreak before the animals of the vicinity have developed any degree of natural immunity to the infection Here the animals present symptoms of cerebral apoplexy They reel and fall bloody liquid flows from the body openings and death soon follows If the body is opened and search is made for evidence of disease it may be quite impossible to detect any definite lesions or change in the tissues

"The acute form of the disease develops more slowly but becomes well established in twelve to twenty four hours after the premonitory symptoms are noticed In these cases the fever is intense (104 to 107°F) The animal is greatly prostrated Cerebral congestion causes excitement which is followed by drowsiness and staggering gait *There is frequent passage of bloody urine followed by convulsions* and death In this type of the disease as well as in the apoplectic form post mortem examination of the carcass may fail to reveal any definite lesion

"*The third form of anthrax the subacute is the most common* The symptoms are like those of the acute form except that they are of slower development Instead of becoming established in twelve to twenty four hours one to seven days may be required The fever is very high Serious colics are often present Local anthrax tumors appear externally first near the shoulders neck and head and are usually due to local injury or bruising which gives rise to a collection of bacilli within the blood vessels of the part whose resulting

inflammation gives rise to the swellings or carbuncles These tumors are at first hard and circumscribed but later become cold insensible diffuse and fluctuating An examination of the carcass of an animal dead of the subacute form will probably show many lesions or alterations Hemorrhages may be found in almost all parts of the body Serous infiltrations may be present beneath mucous membranes and skin There will be swelling of the spleen the liver and the kidneys and the blood will be of a muddy or tarry appearance and incoagulable The cavities of the body contain more or less bloody effusion and the lymphatic glands are swollen and contain small hemorrhages The red blood cells have become broken down *in large numbers* and *the serum of the blood has been markedly* reddened The walls of the intestines may appear perfectly normal but hemorrhages are frequently seen especially in the walls of the duodenum

"The subacute form is the one most commonly met and is the only form which responds favorably to treatment Death ensues so quickly in the other two forms that attempts at treatment are of but little use

Isolated or sporadic cases are usually of the subacute form and are frequently limited to the formation of a tumor or carbuncle at the point of the body at which the infective germs first gain their entrance

ANTHRAX IN MAN

The number of human cases of anthrax in the United States is not large Figures gathered from various state health departments by Smyth (24) would indicate that there are probably less than a hundred cases annually In the first decade of this century British authorities placed anthrax mortality in Europe at about 25 per cent (30) Holtzmann (31) showed German experience in the tannery industry for the period 1927 1932 to average 9 3 per cent fatality as compared to 12 per cent for the same industry in the United States during the same period (24) Anthrax fatalities in the United States (24) *have decreased from approximately 20 per cent in the 1910* 1920 period to about 8 per cent in the 1939 1943 period This improvement has occurred almost entirely in the tannery and woolen mill cases which have shown better than a 50 per cent decrease in fatality *rate over a period of twenty years this rate now being* between five and six per cent in these industries This drop is un

Table 11—ANATOMIC DISTRIBUTION OF PRIMARY ANTHRAX LESION IN 937 CASES (LEGGE)

SITE	PERCENTAGE DISTRIBUTION
Head and face	44 6
Neck	31 2
Upper extremity	20 4
Lower extremity	1 9
Trunk	1 9

doubtedly due to earlier diagnosis and more prompt and efficient treatment Most of these cases occur in large plants having their own plant physicians and trained foremen who are on the look out for the slightest lesions Such plants are for the most part located in or near medical centers where adequate medical service can be obtained promptly Similar improvement in fatalities from other sources in which diagnosis and treatment are usually delayed such as in longshoremen agricultural workers and nonindustrial cases (i e shaving brush cases) have not been noted and remain from 20 per cent to 50 per cent

Human anthrax infection is usually through a skin lesion generally a slight abrasion scratch or small wound on an exposed surface producing primarily the local lesion of malignant pustule carbuncle or charbon Less frequently infection may enter the upper respiratory tract in the form of dried spores in dust from wool sorting or from storage lofts for dried skins or hair and produce the massive pneumonia of woolsorters disease Less often still in man internal anthrax may take the form of an intestinal infection resulting from the ingestion of improperly cooked meat Milk is rarely responsible for human anthrax infection as infected cattle are usually too ill to be secreting milk

Solowieff (32) reporting autopsies on 22 cases of intestinal anthrax states that the lesions are usually limited to a comparatively small section of the bowel most frequently the cecum and adjacent part of the small intestine Jean (33) reports one case of renal anthrax with multiple kidney abscesses unsuccessfully treated by excision

Occasionally no portal of entry is recognizable and infection may localize or at least predominate as a meningitis Cernainu (34) states that the brain is much more receptive to anthrax bacilli than the skin McCowen and Parker (35) report a fatal case of anthrax meningitis with no evident external lesion Several similar cases have been noted in the United States

Internal anthrax of any type is usually fatal although prompt energetic treatment may occasionally be successful One case has been reported (36) of pulmonary anthrax in a two and one half year old child diagnosed by finding anthrax organisms in the sputum The child recovered under serum therapy but with damaged vision the eyes apparently being affected at the start Another case of pulmonary and intestinal anthrax developing after a primary ankle lesion recovered after treatment with serum and arsenicals (24)

The external form of anthrax presents a very typical clinical picture In two or three days after contact with infected material a small reddish blister appears surrounded by an area of erythema At this stage diagnosis is not always easy unless the serous fluid is examined bacteriologically This should be done at once since early diagnosis is of the most extreme importance Clinical diagnosis becomes almost certain however within 24-48 hours with the very characteristic further development of the lesion The center becomes infiltrated and dark red increasing rapidly in size and the center soon becomes black In fact the name *anthrax* is derived from this characteristic black center The lesion may become nearly two inches in diameter surrounded by a wide area of oedema which later becomes hard but not particularly painful unless touched Systemic manifestations fever and prostration often occur out of proportion to the size of the lesion If adequate treatment is not instituted early infection tends to spread rapidly through the lymphatics to the circulation resulting in an almost always fatal bacteremia Square ended rods may be cultured from the local lesion if discharging from serum from the oedematous area and later or post mortem from the blood and internal organs as liver spleen kidney etc If the carbuncle has a sloughing necrosed centre the rods will contain central spores but otherwise organisms from body tissues do not show spores when freshly stained

The most usual sites for local lesions are the head neck and upper extremities being the most exposed areas Legge s Industrial Maladies (17) gives the distribution of primary lesions in 937 cases reported in England (table 11)

Osborn s Massachusetts figures (21) correspond to these except that neck lesions were more frequent than head and face These give more detailed distribution areas Smyth reports as to the location of primary lesion in 640 cases (table 12)

Human anthrax may be derived from direct contact with animal

secretions excretions or infected tissues, or by contact with animal products as hides skins or hair or may be transmitted by biting flies from animals to man

Table 12—LOCATION OF PRIMARY ANTHRAX INFECTION IN 640 CASES (SMYTH)

Total internal anthrax		11	1 7% of total
Pulmonary	4		
Pulmonary and intestinal	2		
Intestinal	2		
Meningeal	3		
Total external anthrax		629	98 3% of total
Face head and neck	309		49 1% (of external cases)
Upper extremity	264		42 0
Lower extremity	23		3 65
Chest abdomen and back	23		3 65
Multiple lesions	9		1 4
Not stated	1		0 1

During the years (1919 43) covered by the Smyth reports (24) few human cases have been reported in the United States as attributed to infection from animals other than sheep cattle horses and mules and none from animal products other than hides and skins of cattle goats horses and mules horse hair, imported wool blood meal and fertilizer As yet no cases have been traced to hogs or hog bristles Many cases were reported due to skinning or autopsying cows shearing sheep butchering and milking Other cases occurred in rendering plants and from the use of fertilizers the material in one instance being wool waste Cases were reported from cattle feed in one instance a blood meal one case developed in a cordage factory from handling sisal fibre from Mexico probably *infected from animals One girl in Louisiana apparently developed* a fatal case while carving statuettes from horse bones One man became infected while caring for a dog that had fed on a dead sheep another while caring for a sick mule The recent cases contracted from minks have already been mentioned. One man thought he became infected from frog hunting but being a Mississippi farmer he was more likely infected from farm animals Another man who had intestinal anthrax blamed it on eating a wild rabbit but according to his physician he was a sheep herder and more likely infected *from dust from sheep Still another case of a dress clerk in an* Ohio store was laid to bites from her pet cat but the cat was not shown to be infected and no source seemed evident

There are a few cases on record where anthrax has passed from one person to another but they are comparatively rare One case

was reported of a three year-old child contracting ocular anthrax while sleeping with her father who had an anthrax lesion (24) There have been several instances reported of familial anthrax (24) In Pennsylvania in 1930-31 in a family on a small farm seven cases developed The first case was reported as small pox with multiple skin lesions rather unusual but died of meningitis with anthrax organisms isolated from the cerebrospinal fluid the second case overlapping the first and also fatal was first diagnosed as erysipelas a third case with multiple skin lesions and anthrax bacteriemia recovered after serum treatment as did four other subsequent cases All seven cases occurred in two months with a return case in the next year in one of the four Recurrences have been reported by three other writers (37 38 39)

Bites of bloodsucking insects may at times be a factor but such cases often can be traced to an infected animal rather than to an infected person upon whom the insect has previously fed

Bites from pets which have recently fed upon the carcasses of animals dead of anthrax have been known to cause anthrax infection This again is of animal origin

Contact with the animal may be quite direct as a farmer caring for a sick animal or skinning one which has died from the disease It may be more remote as handling hides which have been shipped long distances Cases are recorded of workmen in tanneries carrying the infection home to members of their families though escaping themselves Such a happening may be due to a housewife mending or washing her husbands work clothes and the fact that this has occurred is a strong argument for having work clothes autoclaved and laundered at the work place The contact may be very remote such as a man living in a hotel in a large city and rarely even seeing an animal becoming infected by a shaving brush made from hair of an infected animal in China

ANTHRAX AN INDUSTRIAL HAZARD

Human anthrax in the United States is primarily an industrial hazard. Workers in the hide skin leather hair and wool industries show a greater number of cases than in other occupations followed by transportation workers farmers and veterinarians

Statistics collected by Smyth (24) from 1919 to 1943 showed that in the first five year period the majority of cases were in tanneries nearly all of which are located in Delaware Massachusetts

secretions excretions or infected tissues or by contact with animal products as hides skins or hair or may be transmitted by biting flies from animals to man

Table 1? —LOCATION OF PRIMARY ANTHRAX LESION IN 640 CASES (SMYTH)

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Intestinal	2		
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Face head and neck	300		49 1% (of external cases)
Upper extremity	264		42 0
Lower extremity	23		3 6?
Chest abdomen and back	23		3 65
Multiple lesions	9		1 4
Not stated	1		0 1

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There are a few cases on record where anthrax has passed from one person to another but they are comparatively rare One case

normally have few or no cases It is to be expected that following the close of World War II with increased activity in goat skin tanning and increased importations of bales of goat skins which may have been long stored under favorable conditions for anthrax bacilli growth and therefore permeated with bacilli there will again be a decided increase in tannery anthrax

Very few cases in this country have been reported due to finished leather and none of these were proved by isolating the organism from the leather In one case finished leather was shipped to a wooden heel factory where one of the employees developed anthrax and in another anthrax developed after a glove finger stuck to a lesion made by treating a wart Smyth has always been skeptical of anthrax spores surviving the usual tanning processes and as far as is known none of the cases reported as due to finished leather have been proved by the isolation of the organism from the leather

Contrary to the tannery situation that in the woolen and hair industries showed an increase in anthrax during the depression period in spite of decreased activity With increased activity due to war demands the number of cases shot up to 237 in the 1939 1943 period from 51 in the previous period The reason for this increase will be seen in a quotation from Smyth s 1927 report which stated that a marked increase in wool anthrax in this country was predicted when Great Britain opened her disinfecting station in Liverpool (in 1921) All wool and hair that enters England from countries where anthrax is indigenous must pass through this government station and be disinfected before it reaches the industrial plants This is done at a fixed charge which is paid by the importer It was predicted that this practice would result in diverting considerable wool coming from anthrax infested regions and likely to be infected itself and that we would in this country receive a good deal more of this infected wool than we did previously Apparently this is the condition and is a strong argument for the establishment of our own disinfecting station for wool and hair"

One case was attributed to carrying finished rugs although no organisms could be isolated from the rugs Another was attributed to rags imported from Europe for use in paper making Various cases were attributed to scoured and so called sterilized wool the sterilizing" process used being inadequate The outbreak of seven cases with one death in a small primitive industrial village in Pennsylvania among wool carpet yarn mill employees (24) was reported

New Jersey, New York and Pennsylvania While the percentage of tannery cases dropped from 53 in the first five year period to 19 in the last five year period anthrax due to contact with wool and hair increased from 15 to 58 nearly all of these occurring in woolen mills in Massachusetts, New Hampshire New Jersey New York and Pennsylvania with over half of such cases in the last period occurring in Pennsylvania Agricultural anthrax or anthrax due to direct contact with infected animals, has also appeared to increase over the years and to be recognized in an increasing number of states although much of this apparent increase may be due to better diagnosis and reporting While such cases may appear wherever animal anthrax is known (which is practically in every state in the country as shown in table 10) the largest number of cases seem to occur in California Louisiana Texas and probably Mississippi whose reporting is not satisfactory

In Pennsylvania over a twelve year period (1910 21) Smyth and Bricker (40) found that among 13 339 men working in tanneries, 1 040 were directly exposed to infection and of this latter number 123 cases of the disease developed a rate of about 11 per cent

While there has been an apparent decrease in tannery anthrax the degree of anthrax hazard in industry varies with the degree of prosperity and its resultant industrial activity During the long depression period the decreased industrial activity doubtless accounted for the reduction in anthrax cases while during the war period the demand was largely for the more durable cattle hide leathers and relatively few goat skins were processed Goat skins are by far the greatest source of tannery anthrax being imported from countries where anthrax is more or less prevalent and are always likely to have anthrax infestation in some of the skins in spite of consular certification that the area from which they were shipped was free from anthrax at the time Smyth has personally isolated anthrax spores from various skins so certified The large cattle hide tanneries have very little anthrax since most of them are packer controlled and nearly all of their raw material comes from healthy cattle slaughtered for food under Government supervision During prosperous periods however, with greater demand for leathers many hides collected by traders through the country or on the ranges come to tanning and with them comes anthrax as Smyth has personally observed (24) These tanneries are smaller and more widely scattered and less likely to be on the outlook for anthrax since they

of 35 000 allegedly sterilized brushes from Japan A personal communication from the North Dakota Health Department stated that investigation by them and the United States Public Health Service showed that a considerable proportion of these were contaminated by anthrax spores Many of this shipment were traced and withdrawn from sale In the 1939 1943 period there were no cases reported from this source although two cases were attributed to a hair brush and a toothbrush

As an illustration of the way in which such shaving brush infection may remain for years a latent danger the London Letter of the Journal of the American Medical Association for August 10 1935 notes that three years previously a consignment of 12 shaving brushes came into Lambeth and was found infected Eleven were seized but the twelfth had been sold and could not be traced Every one of the eleven contained anthrax Eventually the twelfth brush was found but unfortunately not until after causing a fatality A boot repairer had used this infected brush daily for two years at last becoming infected only after cutting himself One other case was also reported in 1935 (45)

PREVENTION AND CONTROL

The prevention and control of anthrax in man depends upon three factors eradication of the disease in animals elimination of industrial infections and finally earlier diagnosis and more prompt and energetic treatment of infected cases

The eradication of anthrax in animals is a difficult task but is being accomplished as an economic measure in the animal industry Vaccination of sheep horses and cattle in infected areas is the most useful measure known Such vaccinations do not afford protection for more than a year and must be repeated

Pasteur in his early work used for a vaccine live anthrax organisms attenuated by growing at high temperatures In 1902 Sobernheim used living virulent anthrax bacilli at the same time giving an injection of anti anthrax serum Eichhorn (46) in the United States has prepared a spore vaccine of Pasteur s No 2 strain (attenuated to kill a guinea pig but not a rabbit) which is used together with a potent anti anthrax serum Kelser (47) believes that in heavily infected districts a greater immunity is required than that obtained with the Pasteur No 2 strain and recommends a more virulent strain

At the Veterinary Congress in 1934 there was considerable discus

in 1934 Cases have also been attributed to the use of wool wastes as fertilizers

Hoffmann (42) in Germany reports finding anthrax bacilli in the textile industry on goat hair on textile machinery and on finished yarn One cannot help wondering if with the decided increase in anthrax in the woolen industry in this country some of the untraced cases here may not have been infected from clothing

Industrial anthrax infection may occur in those workers not directly handling infected skins hides wool or hair Smyth in his 1934 report lists four cases in mechanics infected while doing repair work a machinist and a carpenter in Massachusetts a paint cleaner in New York and a stock yard worker in Kansas One case is also given of a New York laborer cleaning out a sewer one of an insurance inspector in Massachusetts two of laboratory workers and one of a man presumably infected from handling a fertilizer in Maine

ANTHRAX FROM SHAVING BRUSHES

During World War I and in the years that followed there was much excitement over anthrax from shaving brushes both in this country and in England The source of nearly all the hair for shaving brushes was horsehair from Siberia and China where anthrax was quite prevalent (43) During the course of shipment in normal times the material was cleaned and disinfected usually in France or Germany With the advent of World War I shipments were made directly to the United States across the Pacific Faulty or careless processes for insuring protection against the disease were responsible for a considerable number of cases

The first recorded case of anthrax from a shaving brush was on July 9 1915 in a British soldier (44) From that time on similar cases occurred not infrequently in both the British and American forces as well as the civil population In the United States troops there occurred during the war 149 cases of anthrax with 22 deaths due to shaving brushes In New York City from 1919 to 1923 there were 32 cases reported from this source In Illinois Hull examined one lot of three dozen brushes every one of which was contaminated with virulent anthrax spores

This hazard formerly so widely spread and justly feared and guarded against had until 1938 very materially lessened due to stringent regulations as to the sterilization of hair for brushes Another outbreak however occurred in 1938 39 traced to importation

tion in pure culture is recommended The following procedure is suggested

Make broth culture of suspected material incubate 24 hours heat and hold in water bath at 80 C for 10 minutes to kill non spore formers

Inject 0 5 to 1 0 c c subcutaneously in abdomen of guinea pig Pig may die in from 24 hours to 7 days Hold inoculated animal under observation 8 days before regarding as negative If pig dies immerse completely in 10 per cent formaldehyde for a half hour before autopsy and autoclave cage before cleaning

Autopsy if positive should show gelatinous edema at site of inoculation increase of serous fluids and congestion of internal organs especially large dark friable spleen Gram positive irregularly stained square ended rods single or in short chains without spores should be found in smears from edematous area cut surfaces of liver kidney and spleen and from heart blood Confirm by characteristic colonies on agar and by growth in bouillon gelatin and litmus milk

Always confirm diagnosis by inoculation of second guinea pig with pure culture isolated from heart blood or from liver spleen or kidney The second animal should die in from one to four days with the same findings as the first (For further details of laboratory diagnosis see Stein 23)

In Europe however much dependence seems to be placed upon the Ascoli precipitin reaction (50) rather than animal inoculation This reaction depends on the use of a heat stable antigen obtained from organ extracts of animals dead from anthrax and probably containing specific polysaccharides from encapsulated organisms These extracts give a precipitate with anti anthrax serum (51)

The elimination of industrial infections depends chiefly upon the proper disinfection of all raw materials likely to be infective the disinfection of the workplace and the education of employers and employees as to the need of prompt care of all skin wounds among workers liable to infection

The primary consideration should be the prevention of infective materials reaching the workplace which of course concerns chiefly the disinfection of wool hair skins hides etc Many devices have been suggested for the sterilization of hides none of which have been entirely satisfactory Two considerations are of prime importance economy of cost which will make the process come within

sion and favorable report on the use of the so called Carbazoo vaccine devised by Mazzucchi (48) *This consists of a suspension of a* virulent anthrax culture in saponin The saponin encourages early formation of gelatinous edema at the site of injection which acts as a barrier against the rapid dissemination of the bacilli This was given its first practical test in 1929 It was then freely distributed in Italy and between 1931 and 1934 over ten million animals were vaccinated some in heavily infected areas No deaths were recorded in these districts from vaccination or from natural infection Eichhorn (49) reported over 500 000 vaccinations in the United States with *equally good results This vaccine has since come into use in most* European countries parts of Africa and Japan

Stein (23) *of the* U S Bureau of Animal Industry states

The selection of the anthrax biologic to be used on a given lot of animals *should* be left to the local veterinarian or State Livestock sanitary officials who because of their experience and knowledge of the local *conditions* are in a position to know which products are best suited to the needs of the herd Each of the immunizing agents mentioned has a particular field of usefulness and also definite limitations

Fields *once infected* with anthrax bacilli are difficult to cleanse These should be *turned to other purposes* than grazing wherever *possible Earthworms which were once thought to be a factor in carrying anthrax spores from the depths of the soil to the surface are probably not a factor* in the spread of the contagion *Animals* dead of the disease should not be carried to new localities *but should be* disposed of on the premises They should either be burned or buried deeply with quick lime without opening the carcasses or removing the skins In the absence of oxygen spores are not easily formed and the vegetative forms of the organism are easily destroyed When the skin is opened spores form with the access to oxygen and the problem of destruction is greatly increased However any regulations requiring the proper safe disposal of the carcasses of animals dead from a transmissible disease must *fail* to *produce* the desired result unless the said disease is diagnosed ante mortem More than one cattleman or other animal owner has be*come* infected from autopsying an animal for the purpose of making a diagnosis

For the recognition of anthrax in suspected materials as animal tissues hides skins hair etc the use of culture methods for isola

tion in pure culture is recommended The following procedure is suggested

Make broth culture of suspected material incubate 24 hours heat and hold in water bath at 80 C for 10 minutes to kill non spore formers

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the possibility of commercial use and lack of injury to the hides and skins Horsehair and wool can be sterilized quite satisfactorily as is done at the central disinfecting station in England

The government disinfecting station at Liverpool (41) is planned

ANTHRAX

A CURABLE Infection if Treated in Time

NOTE THE THREE STAGES

DO NOT LET IT PASS THE FIRST STAGE

1st STAGE

2nd STAGE

3rd STAGE

NEVER Touch a Pimple or Sore until the hands are carefully washed

WASH in Bichloride Solution or other Solution provided for the purpose of preventing infection

REPORT at ONCE to the Superintendent the first Indication of infection ANY Indication is IMPORTANT

Fig 17 —Copy of a poster used by the United States Department of Labor to safeguard workers in the tanning industry

to receive all wool and hair imported from countries where anthrax is prevalent Material is washed in a hot alkaline suds in a wool washing machine followed by a hot 2 per cent formaldehyde solution and storage for several days in a holding room The British feel that such a central cooperative government plant is the only safe and sure means of disinfecting raw wool and undressed hair as the small dressers and spinners will not and can not carry out proper methods

In the United States government regulations (52) originally required the disinfection of horsehair and wool from suspected sources by subjection to dry heat at 165 F for 15 minutes but inspectors now require a 24 hour holding period preceded by washing in hot nearly boiling alkaline suds Autoclaving with steam under pressure is much more certain than this but may be objected to by some manufacturers using horsehair for brushes for fear of setting a curl in the hair The English formaldehyde method is much more satisfactory

The problem of disinfection in tanneries is a more difficult one because of the possibility of injuring the hides in the process No thoroughly satisfactory method has as yet come into general use in the United States The English Seymour Jones method (53) of soaking for 24 hours in a 1/5000 bichloride of mercury solution with 1 0 per cent formic acid requires a two weeks holding period after treatment to insure success The Austrian Schattenfroh method (54) of soaking in a 2 per cent hydrochloric acid and 10 per cent sodium chloride solution for 48 hours at room temperature can be depended upon to kill anthrax spores but it leaves a harsh skin which is hard to tan satisfactorily

Besides the Schattenfroh method the U S Bureau of Animal Industry (52) has also permitted disinfection of goat skins in a milk of lime (15 lbs burnt lime or calcium hydroxide per 100 gallons thus making at best a 2 per cent calcium oxide suspension) for 12 hours and of cattle hides in 1/1000 bichloride solution for 12 hours neither of which methods can be depended upon to disinfect completely (55)

Smyth (13) has shown that iodine 0 5 to 1 0 per cent or iodine vapor will completely disinfect hides without injury in two hours The cost was at the time his work was done (1923) prohibitive but since this work was reported the price of iodine has dropped to only a fraction of its former level and will probably drop still more

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Fig 17 –Copy of a poster used by the United States Department of Labor to safeguard workers in the tanning industry

taken out of the tannery unless first disinfected The best method of disinfection is by steam under pressure in an autoclave using 15 pounds pressure for 30 minutes

Tannery workers and workers in hair and uncombed wool should be required to wash their hands thoroughly with soap and hot water before lunching and they should take showers before changing to street clothes Adequate washing facilities should be provided A Philadelphia tannery has a washroom and shower room located between the locker room for street clothes and the room where work clothes are put on and taken off When not in use work clothes hang on pegs in the open room in order to dry Workers should not be permitted to take lunches into the work rooms but should be provided with lunch tables and chairs or benches in a room separated from the working area

Employees should be instructed to pay attention to every skin wound even the most trivial and to apply to the plant dispensary or a near by physician to have such skin breaks disinfected at once (iodine is excellent for this) and covered with a protective dressing These should be kept under observation by physician or nurse until completely healed No one should work with unprotected open wounds of any kind If the wound cannot be properly covered by an impervious dressing rubber finger stall or glove the employee should quit work until it is healed Skin infections cannot occur through unbroken skin Cuts after shaving should be properly protected and workers should be instructed to keep their hands away from their faces while at work especially if they have cuts or open pimples on the face

The successful control and cure of those cases developing where adequate protection has not been afforded depend upon early diagnosis and prompt efficient treatment

While in the well established anthrax pustule diagnosis can be made by inspection yet wherever possible diagnosis should be confirmed bacteriologically by the finding of irregularly stained Gram positive rods in the secretion from the wound or in serum obtained from a small puncture into a forming lesion or when bacteriemia has developed in a blood smear When in doubt surely and always if possible morphologic diagnosis should be confirmed by isolation of the organism in pure culture and by animal inoculation Freshly isolated virulent anthrax should kill a guinea pig in one to seven days usually under four days After the death of the animal

In view of this this work should be carried further in an effort to prove its feasibility on a commercial scale

Robertson (58) in 1932 reported excellent results in the disinfection of dry hides with hydrogen sulphide gas but long exposures were necessary to insure results (7 to 16 days depending upon temperature) No statements are given as to gas concentration and no tests are reported on a commercial scale

Provided a generally satisfactory method for disinfecting skins and hides can be developed it should be carried out in central government stations at ports of entry or even better at disinfecting stations under international management at the shipping ports of countries of origin for the greatest protection of all handlers

Since we have not thus far succeeded in preventing infective material from reaching the workplace our second consideration must be to prevent the worker from becoming infected

In tanneries soak vats are likely to hold infection once acquired over some time These should be periodically completely drained scrubbed thoroughly whitewashed and allowed to be idle for one or two days At the same time the platform around them and under the milling drums should be whitewashed and the drums rinsed with strong milk of lime Lime is suggested because, though not killing all spores it will greatly reduce their number and residual lime will not harm skins that go into liming vats later

In an effort to protect potable water supplies the U S Bureau of Animal Industry asked tanners who did not regularly disinfect skins to disinfect their effluents with liquid chlorine but this is far from economical owing to the high chlorine demand of the organic matter present and incidentally it offers no protection whatever to the tannery workers It requires up to 250 parts per million available chlorine but Tilley and Chapin (56) obtained effective disinfection of effluents with chlorinated compounds getting results with 50 parts per million available chlorine in di chloromethylamine and di chloroglycine

As a protection to the consumer MacDonald (57), on the basis of experimental work recommends the sterilization of carpets in the factory on the sizing machine with the use of hot formalin solution This again offers no protection to the factory worker making the carpet

Clothing worn by workers in wet processes and by handlers of untanned skins especially in goat skin tanneries should not be

so treated For thirty or forty years serum remained the most effective treatment known and was emphatically recommended as the treatment of choice

The early practice of combining excision or cauterization with the use of serum which is still sometimes practiced is to be condemned Another practice usually carried out until a decade or so ago was the injection of serum about the lesion as well as its administration intravenously but the generally accepted policy today is one of "hands off the local lesion Immobilization of the patient during the infective stage to avoid possibility of blood stream infection has always been considered important by practically all physicians who have treated any number of cases Nevertheless in spite of these two widely accepted policies one physician who has within the past three years successfully treated some thirty cases by one method strongly advocates only local injections of 10 15 c c amounts of serum about the lesion repeated in 24 hours if indicated the total amount depending upon the size and response of the lesion In eight of these cases so treated he reports no time lost from employment and in several others the time lost was less than one week

The recommended treatment with anti anthrax serum is 10 20 c c intravenously as a desentizing dose followed by 50 100 c c in two hours If indicated the larger dose may be repeated in 24 48 and 72 hours depending upon the spread of the vesicles and the swelling of surrounding tissues

Severe serum reactions very frequently result either immediately after administration of the first dose or from five to ten days later and for this reason many physicians now prefer chemotherapy to serum

In 1917 Penna et al (65) in Argentina reported the use of non specific normal beef serum with good results and in 1926 Villegas Ruiz (66) reported similar results with the bacteriophage of D'Herelle These treatments were apparently not adopted in this country

In 1926 and 1933 two British writers reported on the use of neoarsphenamine Pijper (67) obtained excellent results with neoarsphenamine alone and Eurich (68) treated over 200 cases with combined serum and neoarsphenamine with a fatality rate of 5 per cent Meshtschaninoff (69) treated 21 patients successfully with neoarsphenamine In this country arsenicals were not used before

the organism may be isolated from all body tissues and fluids When anthrax is suspected however treatment should not be delayed pending positive diagnosis, but begun at once

As to the most effective means of treatment developments in new methods are progressing so rapidly that any recommendation made here might well be outmoded almost before publication

In the early days of anthrax the recommended treatment was the removal or destruction of the lesion by excision cauterization or injection of 50 per cent phenol about the lesion This was however soon found more or less ineffective especially when not properly carried out or carried out too late Often the infection was spread to other tissues through such manipulation

After Koch s discovery of the anthrax bacillus in 1876 (6) Pasteur (59) successfully vaccinated sheep against the disease in 1880 and about the same time Toussaint (60) discovered that blood from animals dead of the disease when heated and injected into other animals would protect them against infection Vaccination of animals has been successfully carried out since that time but as this is accomplished by the use of attenuated cultures (killed cultures not being very effective) humans are not vaccinated against this disease because of the danger of occasional increase in virulence of the culture

In 1895 Marchoux (61) in France prepared an efficacious anti anthrax serum which would cure sick animals but because of the more acute course of the disease in animals than in man even today treatment of animals with serum is not too successful and not prevalent It is worth trying however if the animal is highly valued or it may be that sulfa drugs may soon prove useful in treating animals These are discussed later

In 1895 Sclavo (62) in Italy produced a serum that has been widely used for the cure of anthrax in man His original serum however has been modified by the use of ass serum instead of horse serum In this country today we use an anti anthrax serum produced by inoculating horses with virulent organisms With the advent of this specific serum the fatality rate for anthrax was cut sharply Sclavo (63) in 1903 published statistics showing a fatality of 6 per cent in 164 patients treated with serum as against 24 per cent for Italy as a whole In 1911 the British Ministry of Health (64) in a report on 800 cases of anthrax gave the fatality rate for serum treated cases as 4 per cent against 48 per cent for those not

ment were given 15 000 units were given intramuscularly every three hours for one week smears appearing negative for anthrax bacilli in 24 hours and cultures proving negative after four days

Except for those cases treated by serum alone the following figures may be considered only suggestive since no rates should be based on less than 200 cases for any degree of accuracy but they do give some idea of results obtained by various treatments from case records sent in to Smyth

Treatment	No of Cases	Fatality Rate
None wrong diagnosis	25	88 per cent
Non specific local treatment incision excision cautery	60	28 3
Serum only	519	8 6
Arsenical only	62	0
Sulfa Drugs only	64	4 7
Serum and Arsenical	72	8 3
Serum and Sulfa Drugs	32	9 4

Lucchesi (70) gives the following criteria for the ideal treatment

1 It should not harm the patient
2 It should produce the lowest mortality
3 It should cause the shortest absence from employment
4 *It should be the least expensive*
5 It should be easily given

And to this we would add that it should be readily available

It would seem from the information at hand at present that to meet these requirements neoarsphenamine would be the treatment of choice Serum is not always readily available and promptness of treatment is extremely important It is also costly and produces more or less severe reactions While sulfathiazole is easily administered by mouth and meets the requirements it must be administered every three or four hours for perhaps a week as must also penicillin while neoarsphenamine need be administered only two or three times within approximately two days and appears to produce the lowest fatality rate

It might be advisable since promptness of treatment is so necessary to administer sulfathiazole orally at once while awaiting hospitalization *and the administration of neoarsphenamine*

In the woolen mill industry in which 237 of the 408 cases during 1939 1943 occurred the fatality rate was definitely lower than it was for the rest of the country although many cases were treated by each of the accepted methods Since these undoubtedly received earlier diagnosis and treatment than the others it is evident that

1932 and then in only a few cases Since then, however they have been used more extensively with apparently excellent results In a few cases mapharsen and neosalversan were used but the most satisfactory and most widely used arsenical is neoarsphenamine given intravenously 0 6 grams initially and 0 9 grams the following day *repeated in 24 hours if indicated* No *reactions have resulted* from this treatment as with serum and recovery has been more prompt (70)

Until very recently at least it has been considered advisable in very severe cases to combine the use of serum with neoarsphenamine and in such cases smaller doses of each are given than when either is used alone

Of 62 cases for which Smyth has records treated by arsenicals alone none was fatal even though one patient was moribund when brought in Of 72 cases treated with serum and arsenicals six were fatal although one of those recovering had not only an ankle lesion but also a positive sputum and stool It is beginning to appear that serum is not a necessary adjunct to neoarsphenamine for successful treatment

In the past few years sulfa drugs have been quite successfully used In 1939 two papers one by Cruickshank (71) and one by May and Buch (72) on experimental work with mice showed sulfanilamide and sulfapyridine effective in treating these animals Neoprontosil sulfanilamide sulfapyridine sulfadiazine and sulfathiazole *have all been used but the most widely recommended is sulfathiazole* 3-4 grams by mouth initially with 1 1 5 grams every 3 4 hours up to seven days if indicated In 1942 Gold (73) published his results on the treatment of 40 cases with various sulfa drugs He feels that recovery is more prompt with sulfathiazole than with any other treatment and that this is the treatment of choice

Of 64 cases for which Smyth has records treated with sulfa drugs alone three were fatal while of 32 cases treated with serum and sulfa drugs three died although one of those who recovered had a blood stream infection

Very recently penicillin has been used and *may prove extremely* effective although too few cases have as yet been reported to allow any conclusions In August 1945 the American Medical Association (74) approved the use of penicillin in the treatment of anthrax Smyth has records of only four cases so treated with no fatalities In the one case (with lesion on the face) in which *details of treat*

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while there is doubtless some difference in the efficiency of the various methods of treatment the really cardinal factor is the promptness with which treatment is instituted

ITEMS OF NOTE

1 Anthrax is primarily a disease of animals
2 Practically all human infections arise from contact with animals either direct or remote
3 Anthrax in man in the United States is primarily an industrial hazard at the present time but agricultural anthrax is also apparently of increasing importance
4 The anthrax bacillus in its spore stage is among the most resistant of pathogenic bacteria
5 The control of anthrax in man depends upon the promulgation of educational measures among the industrial workers exposed to infection together with better devices for sterilization of infected hair hides and wool and also upon the control of the disease among domestic animals
6 The shaving brush must not be disregarded as a hazard
7 For treatment immune serum arsenicals and sulfa drugs are now being used the treatment of choice probably being neoarsphenamine
8 Promptness of diagnosis and treatment are of even greater importance than type of treatment

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CHAPTER III

BRUCELLOSIS *

Brucellosis is a disease of animals and man caused by one of the three species of the genus *Brucella* The known species of this genus are *Brucella melitensis* *Brucella abortus* and *Brucella suis* The chief host of *Br melitensis* is the goat of *Br abortus* the cow and of *Br suis* the hog Each of the species is infectious for all domestic animals with the exception of *Br abortus* which does not appear to infect hogs

The disease in cattle is known as Bang's abortion disease" *Br abortus* is the species largely responsible for this disease It is characterized by inflammatory changes of the mucous membrane of the uterus and fetal membranes resulting as a rule in the premature expulsion of the fetus A chronic interstitial mastitis is produced in the udder of the cow

The disease in man is known as undulant fever the symptoms being characterized usually by a protracted febrile condition with a tendency toward recurrence Indeed the symptoms are so inconstant and confusing that no one of them can be said to be typical and a differential diagnosis is almost impossible in most cases without serological aid

A multitude of names have been used to describe these conditions in man The following terms are found in the literature associated with the geographical distribution

Malta fever Maltese fever Mediterranean fever Danubian fever Neapolitan fever Rock fever Gibraltar fever Cyprus fever Bang's fever From the clinical manifestations the terms undulant fever and febris undulans have been used because of the wave like recessions of fever and Mediterranean phthisis from the bronchitis

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anemia and night sweats suggestive of tuberculosis Other similar names suggesting clinical manifestations are Bruce s septicemia melitensis septicemia febris melitensis and bilious remittent fever In Texas and New Mexico the terminology has differed somewhat—slow fever goat fever continued fever mountain fever Rio Grande fever and dust fever (because it was supposed infection was con tracted in the dust filled goat pens) The diagnosis is often confused with other diseases which has led to such designations as intermittent typhoid fever or typho malarial fever The diseases for which undu lant fever is mistaken are typhoid paratyphoid malaria tubercu losis rheumatic fever influenza septicemia leptospirosis and some times kala azar and amoebic liver infections

The relationship of Bang s disease of cattle and brucellosis in hogs to human infections has but recently been recognized The diagnosis has usually been mistaken for other diseases as tuberculosis typhoid fever malaria influenza rheumatic fever or articular rheumatism until laboratory examinations of blood serum have proved otherwise

The term undulant fever" is found in the literature to designate human cases infected with any of the three organisms and is gen erally accepted all over the world to describe this form of infection

HISTORY

Undulant fever has probably existed for many centuries Hippoc rates described a disease in man characterized by protracted fever with a tendency to relapse which somewhat resembled tuberculosis and which was not very fatal It is probable that the disease was undulant fever Nothing further is recorded of it however until 1816 when Burnett described it under the name of remittent ma larial fever

In 1863 Marston described it in detail calling it Mediterranean remittent fever In 1886 Bruce isolated the causative organism which Hughes named several years later (1892) *Micrococcus meli tensis* In 1897 Wright and Semple described the agglutination test for undulant fever resulting in a distinct advance in the diagnosis of the disease The first accurate knowledge of its epidemiology connecting the disease with goats was the result of the study of the British Commission for the Investigation of Mediterranean Fever Six reports were put out during the years 1905 1907 It was shown that in the Island of Malta goats milk was the usual source of infec tion in man 10 per cent of the goats were found to be excreting

the organisms in the milk Further tests on small groups showed 50 per cent of the animals were infected

Infectious abortion likewise probably has a record of great antiquity The disease in Europe has been known for centuries where the infectiousness of the malady in cattle together with the losses caused by it are related by Moscall in 1567 by Lawrence in 1805 and by Skellet in 1808 The Complete Farmer in 1807 stated that it is considered certainly contagious and when it happens the abortion should be immediately buried, and the cow kept as widely apart as possible from the herd and not receive the bull that goes with them Numerous other investigators added to the knowledge of the disease during the next century—Jonati in 1837 and Barlow in 1851 St Cyr in 1875 stated his belief in a specific agent and the next year Franck communicated the disease to healthy cows by introducing the discharge and fetal membranes from aborting animals This work was corroborated by Lehnert (1878) and Brauer (1880) Nocard in 1888 isolated two organisms—a short bacillus and a micrococcus—but failed to reproduce the disease in healthy animals with either one

Bang assisted by Stribolt in 1896 discovered the etiological agent which was named *Bacillus abortus* The disease could be reproduced at will with pure cultures of this organism when administered to susceptible animals and from the uterine discharges the same organism recovered Numerous investigators since that time have confirmed these findings

The agglutination test as well as the complement fixation test was first used by several investigators for the diagnosis of the disease in cattle in 1909 and 1910 following the description of similar tests for the diagnosis of glanders in horses Among these were McFadyean and Stockman Holth Grinstead Wall Zwick and Brull

The date that Bangs disease was introduced into the United States is not known but it must have been quite early in the history of the colonies along with imported cattle

The first suspicion that it was related to human health was the demonstration of abortus organisms in cows milk by Schroeder and Cotton of the United States Department of Agriculture in 1911 The same year Mohler and Traum co-workers of the above investigators published the results of the first isolation of the organism from the tonsil of a child In 1913 Larson and Sedgwick showed the presence of agglutinins and complement fixing bodies in the blood stream of

children In 1918 Alice Evans at the United States Department of Agriculture demonstrated the close identity of *Brucella abortus* of cattle and *Brucella melitensis* of goats and later the relationship of the abortus organism to human infection

THE ETIOLOGIC AGENTS

One of the strange occurrences in the history of bacteriology was the failure over a period of more than twenty years to identify two organisms which are so closely related as to be almost indistinguishable Indeed not only was the relationship overlooked but two different generic names were used to designate them this in spite of the fact that the resources of bacteriologists were later taxed to the utmost to find distinguishing characteristics

Brucella melitensis was isolated by Bruce working in the Island of Malta in 1887 as the causal organism of Malta fever of man Ten years later Bang in Denmark discovered *Brucella abortus* as the cause of infectious abortion of cattle *Brucella suis* was isolated from aborted swine fetuses by Traum in 1914 The differences in geographic distribution of the diseases in the animals primarily affected in the clinical manifestation of the diseases and finally in the fact that Bruce incorrectly described his organism as a micrococcus all served as definite barriers against a comparative study of the two organisms

Alice Evans in 1917 working in the Dairy Division of the United States Department of Agriculture began the study which has since proved so valuable in both veterinary and human medicine She was making a study of the bacterial flora of cows milk when the problem of *Brucella abortus* was confronted During a conversation with Dr Eichhorn Chief of the Pathological Division it was suggested that a comparative study of *Brucella abortus* and *Brucella melitensis* be made This was done with the astonishing results that the two organisms were indistinguishable except by agglutinin absorption tests

The nomenclature of the two organisms is confusing Following are some of the designations

Micrococcus melitensis
by Bruce 1887

Bacillus melitensis
by Jordan 1912

Bacillus abortus
by Bang 1897

Corynebacterium abortus endemici
by Preisg 1903

Bacterium melitensis
by classification of Society of American Bacteriologists 1918
Alcaligines melitensis
by Castellani and Chalmers 1919
Brucella melitensis
by Meyer and Shaw 1920

Bacterium abortus
by classification of Society of American Bacteriologists 1918
Alcaligines abortus
by Castellani and Chalmers 1919
Brucella abortus
by Meyer and Shaw 1920

The term *Brucella* has been accepted by the Society of American Bacteriologists and is used in Bergey s Manual of Determinative Bacteriology

The outstanding features of the organisms are their great pleomorphism sometimes assuming the form of cocci (which misled Bruce) and at other times the form of bacilli and the difficulty of separating strains of human bovine porcine caprine or equine origin by morphological cultural biochemical pathological or serological means

In primary cultures the *melitensis organism* is rather easily grown by the ordinary laboratory methods while the *abortus organism* requires an atmosphere of 10 per cent carbon dioxide for the best results *After twelve to fifteen transfers on culture media it will* grow at atmospheric CO_2 tension

The term *paramelitensis,* which is a dissociated phase of *melitensis,* was suggested by Negre and Raynaud to designate those strains which were similar to *melitensis* in morphological cultural and biochemical behavior but failed to agglutinate or agglutinated only slightly in *melitensis* serum *Paramelitensis* organisms absorbed agglutinins from *melitensis* serum only partially

A serological classification of members of the *melitensis abortus* group was made by Evans Among 68 strains of organisms from human bovine caprine porcine and equine sources eight different groups were found by means of agglutinins absorption test The report concludes (1)

"The majority of bovine and porcine strains fell into one large group (33 strains) which is designated variety *abortus* Five strains of human origin were of this variety

Another group important in this country includes strains of human bovine caprine and equine origin (12 strains) It is designated variety *melitensis* A

"Three groups which were found to be prevalent in the Mediterranean countries did not occur among the strains received from countries outside of those regions *One of those groups is designated* variety *melitensis* B another which corresponds with the descriptions of the so-called *paramelitensis* is designated

variety *paramelitensis* another serologic group is designated *paraabortus* because it is serologically closely related to the *abortus* variety and exhibits agglutination peculiarities like those of the variety *paramelitensis*"

Simple agglutination tests cannot distinguish these different varieties and groups

A simple and accurate method for distinguishing the three species of *Brucella* has been devised by Huddleson The method involves the employment of aniline dyes in a certain concentration in tryptose agar which inhibit the growth of one species but not the other Basic fuchsin in a final concentration of 1 100 000 inhibits the growth of *Br suis* Thionin in a final concentration of 1 100 000 inhibits the growth of *Br abortus* The growth of *Br melitensis* is not affected by the two dyes

The three species may also be distinguished one from the other by elementary chemical analysis Although the three species are very closely related serologically no one has yet succeeded in changing one species to another

GEOGRAPHIC PREVALENCE

Br melitensis occurs among goats and man in many of the subtropical countries—in countries bordering the Mediterranean in *South Africa China the Philippines Peru and in Iowa Indiana* Arizona Texas and New Mexico in the United States It has been said that the disease does not exist in Europe north of 46 latitude but outbreaks have been known to occur farther north Evans draws attention to the curious fact however that although goats milk is widely used in Hungary Switzerland Czechoslovakia and Southern Germany the prevalence of undulant fever cannot be compared to that in the neighboring countries to the south

Bang s disease in cattle is widespread It is an important cattle disease in the British Isles France Switzerland Germany Denmark Belgium Austria South Africa the United States Argentina Mexico and Canada Possibly the cause of this is because the cattle industry is more particularly confined to these areas The warmer countries are also afflicted however as reports have come from Italy India Palestine and the Dutch East Indies Infections in man from bovine sources of course follow the distribution of the disease in cattle

Outbreaks of abortion in swine are confined to the middle west and the western coast of the United States

SEASONAL PREVALENCE

There is probably no seasonal prevalence for this group of diseases either in cattle or man in the United States In the Island of Malta there are about four times as many cases of undulant fever in humans during the summer months as during the winter months

BRUCELLA MELITENSIS IN ANIMALS

Goats show no morbid symptoms of the disease Unless man had been infected the disease in goats would never have been suspected Animals fat and in apparently good health will show positive agglutination reactions in the blood during life and at post mortem there can be demonstrated the *melitensis* organisms in the tissues In some instances, when goats die of the disease, there is congestion and degeneration of the liver hypertrophy of the spleen and swelling of the abdominal lymphatic glands and mastitis At other times infected animals exhibit indefinite symptoms such as lassitude loss of flesh cough and lameness Dubois states that abortion may take place in 50 to 90 per cent of the animals when a flock is first infected *Brucella melitensis* is present in the milk urine blood and tissues of infected goats The excretion in the milk may be intermittent disappearing for a week or more at a time then reappearing in enormous numbers

Sheep rank close to goats in susceptibility Cesari (26) recounts that 49 out of 429 sheep at Aveyron gave positive agglutination tests while in two other instances 7 out of 74 and 6 out of 12 were positive

Horses are very susceptible to infection with two of the species of *Brucella* (Fitch et al) (33) The infection is focal in type causing fistula of the withers poll evil and abscesses in the region of the sternum and fetlock In Sicily 20 per cent of the horses gave feeble agglutination reaction while Dubois reports 2 per cent positive tests in horses This does not indicate however actual cases of infection A large percentage of horses will agglutinate the organism slightly

Mules are also very susceptible In the Island of Malta Kennedy found 37 positive agglutination reactions among 87 mules Cesari tells of two men taking care of such infected mules both of whom contracted undulant fever neither of the men had come in contact with goats

Cows have been found naturally infected in the Island of Malta

excreting organisms of *melitensis* in the milk. Evans inoculated a pregnant heifer with a culture of the *melitensis* organisms inducing abortion and obtaining the organism from the fetus and colostrum.

Dogs may give an agglutination reaction to *melitensis* as high as 1:600. In the Island of Malta Kennedy found 9 such reactions among 114 dogs. From one he isolated the *melitensis* organism from a mesenteric gland. Dogs have been found infected with *Br. suis* and *Br. abortus*. Bruce found among 22 cats 5 positive reactors, from the mesenteric gland of one of which he isolated *melitensis*.

Table 13.—SUSCEPTIBILITY OF ANIMALS TO BR. MELITENSIS, BR. ABORTUS AND BR. SUIS (Huddleson)

SPECIES	BR. MELITENSIS		BR. ABORTUS (BOVINE)		BR. SUIS	
	Large D	Small D	Large D	Small D	Large D	Small D
Man	++++	++++	++++	−	++++	++++
Monkey	++++	++++	++++	?	++++	++++
Bovin	++++	++++	++++	++++	++++	?
Goat	++++	++++	++++	++++	++++	++++
Swine	++++	++++	−	−	++++	++
Rabbit	++++	++++	++++	++++	++++	++++
Guinea pig	++++	++++	++++	++++	++++	++++
Rats	++++	++++	++++	+++	++++	++++
Mice	++++	++++	++++	+++	++++	++++
Horse	?	?	++++	++++	++++	++++

Large D = large dose. Small D = small dose.

Rabbits, guinea pigs, rats and mice are susceptible to artificial infection but are not often found naturally infected.

Poultry have been found naturally infected with *Br. melitensis* in France and with *Br. abortus* and *suis* in the United States.

Torstenson (27) observed that cats, dogs, guinea pigs and gray rats kept in contact with infected goats gave negative evidence of infection, indicating that such animals rarely contract the disease naturally, although subject to artificial infection.

Monkeys as well as man easily acquire the disease.

Brucellosis (*melitensis* type) is an animal disease problem in the United States, is found in goats in Texas, Arizona, Colorado and New Mexico, and in hogs in Iowa.

The first experience with the disease in this country was in 1905. The United States Department of Agriculture delegated one of its members to go to Europe to procure a supply of goats with which to build up the milk goat industry. After inspecting several sources, Dr. Thompson selected sixty-one females and four males from the

Island of Malta arriving with them in New York in September 1905 During this time the British Commission for the Investigation of Mediterranean fever had established the fact that Maltese goats were carriers of *Br melitensis* As soon as the British Commission learned of the importation of such goats into the United States it informed the Secretary of Agriculture of the danger The goats were immediately quarantined upon their arrival An investigation made by Mohler and Hart upon the urine and milk as well as agglutination tests of the blood revealed the fact that several animals were infected Efforts to eliminate the disease from the herd so that some of the goats might be saved were unsuccessful and eventually all were destroyed

The fact that *Br melitensis* existed endemically in the United States was not established until 1911 when Gentry and Ferenbaugh (3) discovered the disease in humans in the goat raising section of Texas tracing the infection to goats the blood of which gave positive agglutination tests Mohler and Eichhorn (1) who confirmed the above observations estimated that undulant fever had existed in Texas and New Mexico for at least twenty five years In 1925 Holt and Reynolds (5) of the United States Army investigated twenty two counties in Texas New Mexico and Arizona along the international boundary In seven of these counties no goats were found but in the other fifteen *Br melitensis* infection was demonstrated Four counties north of the border counties were likewise found to harbor infected goats

BRUCELLA ABORTUS IN ANIMALS

Brucellosis or Bang s disease in cattle is the most serious disease next to tuberculosis with which the animal industry has to deal In the United States it exists everywhere in range cattle as well as dairy cattle The economic loss resulting from its ravages was estimated in 1927 by Edwards and Coffee (30) to be eighty millions of dollars annually

In Missouri over a period of ten years 15 000 cattle were tested for Bang s disease 30 22 per cent of which gave positive agglutination reactions (28) At the Storrs Experiment Station in Connecticut 29 1 per cent of cattle purchased reacted to the disease Ninety per cent of the herds in that state were at one time infected In Pennsylvania according to Munce 65 per cent of the cows that were sent to the butcher on account of their failure to reproduce were

sent because of Bang s disease In Michigan 12 per cent of the cattle are reactors to the agglutination test but as Huddleson points out all such animals may not be infected In Illinois about 10 per cent of cattle reacted in 55 herds tested by Graham The Committee on Bovine Infectious Abortion of the American Veterinary Medical Association lists six states as practically free from infection—North Dakota Wyoming New Mexico Alabama Mississippi and West Virginia (6)

The disease in cattle has no particular clinical symptoms except those associated with the act of aborting The health of the cow does not seem to be impaired and the death rate is nil

The most serious consequences of infection are diminished milk supply either through a lessened flow due to the diseased condition of the udder or being dry for a long period loss of calves sterility either temporary or permanent and septic conditions of the uterus or udder disorders due to parturition occurring while the glands are actively secreting *Brucella abortus* has an affinity for embryonic tissues and is present in the uterus of infected pregnant animals After abortion it may disappear from the uterus but can still be found in the udder Here it may remain several years causing serious damage to the milk producing tissue and appearing regularly in the milk It is also found in the uterine discharges accompanying abortion

Bulls are susceptible to infection at times Buck Creech and Ladson (7) found the seminal vesicles of 4 bulls infected out of 325 examined The lesions are often so extensive that permanent sterility results

Infection of swine with *Br suis* was first noted in 1914 by Traum and confirmed in 1916 by Good and Smith (8) from which time it has become increasingly prevalent in the United States especially in the Middle West and on the west coast The strain of *Brucella* responsible for porcine infections is more highly virulent for hogs than is the bovine strain

Sheep and goats have been reported by Schroeder as susceptible to infection with *Brucella* through contact with cattle The animals abort as do cattle Foxes likewise have been reported by MacFadyean and Stockman as aborting when they have come into contact with the infection

Horses are subject to an infection causing abortion which should not be confused with the type of infection discussed here *Salmo*

nella abortus equi is a member of a distinctly different group of organisms

The control and prevention of Bang s disease in cattle is of vast importance economically The extent of infection in any herd may be determined by means of the agglutination test on the blood serum of each animal A single test however is not sufficient to discover all animals harboring the germs Several weeks or months may elapse after an animal has been infected before it shows a positive agglutination reaction The test must be repeated two or three times therefore at intervals of six weeks or six months before all infected animals are eliminated

Herds can be cleared of infection by eliminating the affected animals and carefully and thoroughly disinfecting the premises Subsequent tests should be made to pick up any animals that may have been missed on the first test

Herds that are entirely free from infection may be kept in that condition by strict attention to certain details The disease is usually introduced through the purchase of infected cows or pregnant heifers Bulls and unbred heifers are said to be of less danger in spreading the infection The role of the infected bull at the time of service has been much discussed It is maintained by observers that if the service takes place on neutral ground there is small chance of the cow becoming infected The infected semen from the bull or vaginal discharge from the cow contaminating the premises is of greatest significance The agglutination test should be used before any new animal is admitted to an uninfected herd Other routes of infection are hay and grain produced on farms where the disease exists drainage from an infected pasture bedding from railroad stock cars scattered along the track and neighboring pastures and unpasteurized milk from creameries used to feed calves

The use of vaccines to immunize cows against Bang s disease has received much attention but results so far are disappointing Immunization procedures for adult animals are still in the experimental stage Since 1938 there have been many reports pertaining to the use of a Brucella vaccine developed by Cotton Buck and Smith (34) for the immunization of calves against Bang s disease The vaccine is known as strain 19 It has been conclusively shown that when calves are treated with this type of vaccine a large percentage develop a high degree of resistance against infection and that it persists for one or more years Strain 19 vaccine is now used extensively

in the United States and foreign countries as a means of reducing the spread of Bang's disease in cattle and preventing abortion

HUMAN INFECTIONS

Brucellosis in man according to Bruce is a "disease of long duration characterized clinically by continued fever profuse perspiration constipation frequent relapses rheumatic or neuralgic pains swelling of joints or orchitis bacteriologically by the presence in the blood and organs of *Brucella melitensis* anatomically by congestion of the spleen and other organs" These symptoms however are so inconstant that as Craig states (9) no one of them can be said to be typical of the disease A differential diagnosis is almost impossible in the majority of cases without the aid of the microscope and the serum test"

The human disease caused by *Brucella melitensis* does not differ markedly from that caused by *Brucella abortus* and *suis* The average duration of infection is twelve weeks *Br suis* infection tends to produce abscesses in the glandular tissues and bones The symptoms of one have no special characteristics to distinguish them from symptoms produced by the other type

The *Brucellae* have not been found ordinarily to locate in the genitals of the human race Belyea (10) however describes one such case in which the *Br abortus* was isolated from the vaginal discharge Carpenter reports one case of abortion in a woman due to *Brucella*

The incubation period is from eight to ninety days The patient becomes aware of general malaise muscular pains and fever which is usually higher in the afternoon The course of the disease may drag along for some time being mistaken for any one of several infections such as tuberculosis malaria or typhoid fever Very often there are recurrences of fever after a lapse of several days or weeks of normal temperature

Undulant fever has been of considerable importance in past years as a human affliction in southern Europe and other semi tropical climates While the disease had been prevalent for centuries it was not until 1905 that the goat was definitely linked up with the affliction Following out the suggestion of the British Mediterranean Fever Commission Malta fever among the British military and naval forces stationed on the Island of Malta was entirely eliminated through the single expedient of prohibiting the use of raw goat's

nella abortus equi is a member of a distinctly different group of organisms

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States The patient was an Army nurse and it was presumed that the infection was contracted from caring for sick soldiers recently returned from the Philippines It is entirely possible however that this was a case of bovine rather than caprine origin

The first actual knowledge of endemic undulant fever due to goats in the United States resulted from the investigation of Gentry and Ferenbaugh in 1911 (3) It was established that the disease not only existed at that time in the goat raising territory of Texas but also had existed for some time under such names as goat fever slow fever continued fever Rio Grande fever etc Mexican goat herders attributed the fever to drinking raw goat s milk and escaped the disease by boiling the milk Since that time sporadic cases of the disease have been reported from the Mexican border

The first epidemic of undulant fever on record in this country of caprine origin occurred in 1922 in Phoenix Arizona (13) In April of that year a herd of goats was brought to the city for the specific purpose of selling goat s milk The industry was apparently quite popular the demand rising to 830 quarts daily by June During May June and July cases of an unknown febrile condition kept occurring until August when the definite diagnosis of undulant fever was established and the sale of goat s milk prohibited Among 400 or 500 people who had used goat s milk over a period of four months there were 40 known cases

The relationship of brucellosis of cattle to public health was a doubtful question for several years Credit largely belongs to members of the United States Department of Agriculture for finally solving the problem

In 1911 Schroeder and Cotton of the Bureau of Animal Industry were attempting to demonstrate tubercle bacilli in milk by guinea pig inoculation (14) Some of the injected animals showed lesions that might be mistaken for tuberculosis but which contained no acid fast bacilli Other investigators had also encountered similar lesions The peculiar malady was transmissible through a series of guinea pigs but its cause was not at first apparent At last however there was isolated after many attempts *Bacillus abortus* of Bang The organisms were shown to be quite common in milk and to be excreted over periods of several years duration by otherwise apparently healthy cows Among seventy seven samples of market milk eight or 10 5 per cent harbored the organisms

Mohler and Traum (15) in 1911 attempted to demonstrate the

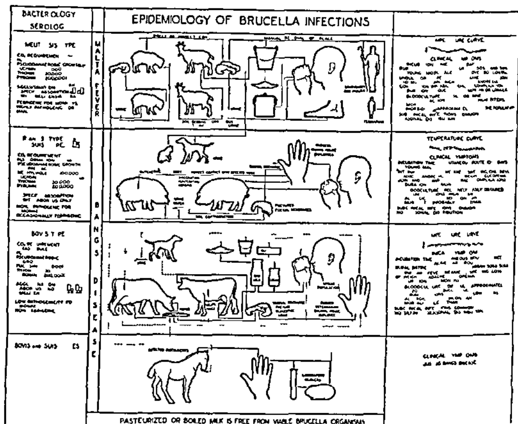


Fig 18—Epidemiology of Brucella infections showing susceptible animals and the methods by which the disease is transmitted (Meyer)

milk The prevalence of the disease in the civil population on the other hand continued unabated Horrocks (11) states that undulant fever practically disappeared from Gibraltar since the practice of importing goat s milk was stopped Stitt relates that on the ship which carried the original consignment of 65 goats from Malta to Antwerp destined for the United States in 1905 several cases of undulant fever appeared among the crew due to milk from these infected animals Two German engineers however who boiled the goat s milk escaped infection

Undulant fever of caprine origin in the United States has never been a serious public health problem From time to time cases of infection originating elsewhere have appeared Tyson describes a case in 1898 the source of infection being Cuba In 1903 Craig described the first case which is known to have arisen in the United

relation of Bang s disease to human infection by means of serologic examination but blood specimens from forty two persons were negative Of fifty six adenoids and tonsils from children inoculated into guinea pigs one specimen produced lesions in the experimental animal from which *Bacillus abortus* was isolated Thus the first human infection was demonstrated

Larson and Sedgwick (16) in 1913 made complement fixation tests on the blood serum of 425 children finding 73 positive with *Bacillus abortus* antigen Agglutination tests run on the same specimens gave parallel results In a later report in 1915 they showed that in the original group of 425 children those receiving milk from an abortion free herd were negative while the children receiving mixed market milk gave a high percentage of positive reactions

The demonstation of *abortus bacilli* in milk and immune bodies in the blood stream of children was confirmed by several investigators

Cooledge (17) in 1916 found among fourteen persons that of six who used raw milk three gave positive blood tests of four using pasteurized milk one gave a positive blood test while of four drinking *no* milk all were negative It was discovered that agglutinins were present in the milk of one of the cows connected with the above study and it was suggested that possibly the ingestion of antibodies from the cow by way of the milk were absorbed into the blood stream and were responsible for the positive tests An experiment lasting over eight weeks where seven persons consumed large quantities of milk rich in antibodies failed to establish the contention

Following the publication of Miss Evans (18) report in 1918 on the identity of the *abortus* and *melitensis* organisms interest in the possibility of human infection from Bangs disease of cattle was renewed but it was not until 1924 that the first authentic case in man was described by Keefer (19) In rapid succession after that other human cases were reported till several dozen were accumulated in the scientific literature by Huddleson (20) Moore and Carpenter (21) Evans (1) Gage and Gregory (22) Knowlton (23) Hull and Black (24) and others

The prevalence of human infection with *Br abortus* is difficult to determine It would appear that possibly it is more common than ordinarily realized Among 69 blood specimens from fever patients which were submitted for the Widal test but found negative Black

Table 14.—INCIDENCE OF BRUCELLOSIS IN MAN

NUMBER OF CASES REPORTED TO THE PUBLIC HEALTH SERVICE BY STATE HEALTH OFFICERS FOR THE YEARS 1935 TO 1943 AND JANUARY NOVEMBER 1944

STATE	1935	1936	1937	1938	1939	1940	1941	1942	1943	JANUARY TO NOVEMBER 1944
Alabama	54	43	48	59	59	70	45	70	63	83
Arizona	4	35	—	31	39	29	21	18	18	27
Arkansas	*16*	35	*30*	*23*	*36*	*21*	*22*	*22*	*13*	*31*
California	150	172	188	243	279	280	318	222	243	308
Colorado	1	3	5	16	37	50	36	12	43	46
Connecticut	59	99	74	96	71	91	123	72	74	56
Delaware	9	—	—	6	3	5	1	—	3	1
Dist of Col	*2*	*1*	*1*	*4*	*6*	*5*	*3*	*4*	*1*	*2*
Florida	68	16	37	42	53	46	21	37	36	28
Georgia	62	60	58	82	121	123	123	129	98	161
Idaho	—	4	14	6	16	7	10	2	1	1
Illinois	144	84	107	212	235	155	217	265	18	311
Indiana	15	15	20	52	58	57	24	31	61	73
Iowa	*112*	*113*	*137*	*124*	*188*	*250*	*354*	*333*	*418*	*282*
Kansas	98	97	82	133	103	170	114	93	179	156
Kentucky	36	46	30	44	19	22	20	18	19	39
Louisiana	49	37	56	60	57	73	64	56	58	49
Maine	20	13	28	26	28	28	33	25	48	35
Maryland	*37*	*41*	*44*	*61*	*59*	*28*	*31*	*29*	*19*	*32*
Massachusetts	42	55	43	37	40	52	86	35	43	44
Michigan	73	89	78	149	252	113	149	121	109	84
Minnesota	115	84	89	87	93	143	180	266	340	303
Mississippi	14	21	23	32	25	30	28	28	42	48
Missouri	69	36	34	32	26	25	32	48	49	37
Montana	11	4	9	7	3	7	11	5	11	13
Nebraska	2	1	2	—	2	17	5	53	5	1
Nevada	1	2	7	2	1	2	2	13	8	4
New Hampshire	1	—	4	6	4	2	16	31	9	1
New Jersey	34	64	67	52	62	76	61	47	71	54
New Mexico	*12*	*11*	*8*	*17*	*13*	*31*	*9*	*4*	*15*	*11*
New York	230	212	190	253	253	255	288	239	286	271
North Carolina	31	23	26	29	25	11	12	9	9	12
North Dakota	2	2	1	8	3	8	7	12	20	2
Ohio	69	79	66	91	91	112	116	77	100	84
Oklahoma	*10*	*96*	*505*	*1 589*	*372*	*112*	*117*	*69*	*30*	*41*
Oregon	19	21	19	22	20	7	23	18	32	40
Pennsylvania	68	86	91	109	121	108	82	74	91	85
Rhode Island	15	12	16	9	18	12	11	9	8	12
South Carolina	11	9	14	28	32	33	11	8	14	18
South Dakota	3	4	2	3	—	4	9	7	25	23
Tennessee	9	26	16	24	*22*	39	27	43	*43*	*51*
Texas	46	43	198	238	327	354	330	231	339	428
Utah	5	3	5	12	28	14	11	7	15	16
Vermont	27	24	44	42	30	44	61	59	47	84
Virginia	39	33	37	50	22	23	16	34	37	35
Washington	35	33	26	40	25	28	47	73	43	54
West Virginia	3	—	7	8	9	5	7	3	3	5
Wisconsin	75	106	94	79	102	114	130	158	178	202
Wyoming	1	2	1	4	13	10	13	9	7	5
Total	2 008	2 095	2 675	4 379	3 501	3 310	3 484	3 228	3 [illegible]41	3 747

results obtained in a state where preliminary testing has shown at least 90 per cent of the dairy herds to be infected with *Br abortus* and approximately 60 per cent of the milk supply only is pasteurized indicate that infection of man with *Br abortus* is relatively rare provided any significance can be attached to the agglutination test (25)

Despite the fact that routine serologic tests do not indicate a high incidence of brucellosis in man in the United States the number of cases reported by state health agencies to the United States Public Health Service continues to increase each year In 1929 only 952 cases were reported while during the year of 1943 3 445 cases were reported

Undulant fever is not confined to adults alone Of the total number of cases reported by the Superintendent of Health of the Maltese Islands during the year of 1936 40 per cent occurred in children under five years of age

In the United States Evans found only 4 cases in children under 9 years of age out of 55 studied The incidence of the disease according to sex depends upon the source and occupation as well as the infecting species In the Island of Malta there is no difference in the sex incidence of the disease In the United States about twice as many cases have been reported in males as in females This is due to the fact that certain occupations bring more males in contact with infective materials

Undulant fever in the United States is a disease that is confined largely to rural sections where milk is consumed unpasteurized or other contact with animals may occur although many cases have been found in urban populations Carpenter studied 155 cases finding that 70 per cent had been drinking raw milk

Hogs have been shown to be a source of human infection with the *suis* organism Miss Evans (1) reports two cases in 1924 one from South Dakota in a meat inspector who had been inspecting hogs for the last eight years and one from Connecticut in a man who had been shaving ears and quartering" hogs McAlpine and Slanetz (29) have found all cultures isolated from man in Connecticut to fall into the *suis* group They also call attention to the fact that the incidence of *Brucella* infection in man is higher in states where the swine industry is large It is possible that cows may become infected with the *suis* species from close contact with swine and thus pass on the infection

and Hull obtained positive *abortus* agglutination tests and histories in five

Several studies have been made to determine the exact status of the prevalence in the human population Miss Evans obtained blood from 500 patients suffering from a variety of diseases whose serum had been submitted for the Wassermann test There were 59 giving

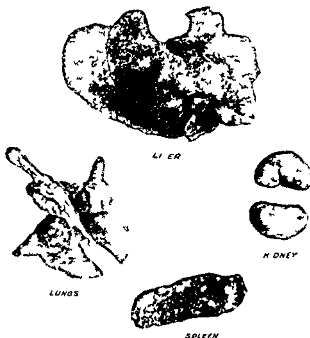


FIG 19 —Lesions in guinea pigs caused by *Brucella abortus*

positive reactions in the 1 5 dilution but not above 1 40 One patient gave undoubted evidence of infection being positive in 1 320 dilution The others were regarded as having ingested infected cow s milk which caused slight infections but not necessarily noticeable illnesses

Litterer in Tennessee tested 1 000 blood specimens submitted for the Wassermann test finding 107 to react in a dilution of 1 10 or greater Carpenter in New York State tested 4 000 similar specimens of which 7 per cent were positive in high dilutions McAlpine and Mickle in Connecticut using routine blood samples submitted for the Wassermann test studied 20 259 specimens finding only 127 or 0 6 per cent positive in 1 100 dilution They conclude that these

chief objection to this agent is the severe inflammatory reaction necrosis and sloughing which occurs in many individuals showing a positive reaction

Brucellergen Allergic Test—Brucellergen was developed in the laboratory of the Department of Bacteriology at the Michigan State College This agent has been studied on more than 20 000 individuals Its accuracy and reliability in detecting *Brucella* allergy is now well established In all suspicious cases or cases in which undulant fever is suspected the first procedure to follow in arriving at a diagnosis is the performing of an intradermal test with Brucellergen

Brucellergen should be kept in the refrigerator when not in use *The vial should be thoroughly shaken before the liquid is withdrawn* The liquid should be removed from the vial under strict aseptic precautions to maintain the sterility of the remaining portion The syringe and needle should be sterilized by boiling

The test is made by injecting about 0 1 c c of the fluid intracutaneously in the lateral surface of the forearm using a 26 gauge needle The local reaction is characterized by a circumscribed erythema edema and induration The size of the local reaction may vary from one to six centimeters in diameter The reaction should be read twenty four hours after injection and again at forty eight hours if the first reading is negative It may persist for seven days There is rarely if ever any necrosis or sloughing of the tissue at the point of the local reaction In the infected the local reaction may not be accompanied by a more marked manifestation of the present symptoms Those who are very hypersensitive will show a systemic reaction along with the local reaction Those who have not been sensitized to Brucella and who are probably susceptible to infection show no local or systemic reaction Often one sees in certain normal individuals an erythema about one half to two centimeters in diameter with no edema around the point of the injection It has the appearance of a non specific reaction

Brucellergen contains phenol as a preservative

System for recording and interpreting skin reactions following intradermal test—

E = Erythema no significance

1 + = Edema and erythema one centimeter in diameter positive

2 + = Edema and erythema one centimeter or more in diameter and mild systemic reaction positive

Studies made by Jordan (32) in Iowa of 1564 cases of undulant fever over a period of seven years show conclusively that contact with infected animals is the most important source of the disease in man The incidence of the disease in farmers who had contact with animals was found to be seventeen cases per 100 000 in farmers wives 0 9 in urban dwellers 0 8 and in packing house workers 131 1

Laboratory workers handling cultures of *abortus* or *melitensis* organisms have become infected from time to time More than the ordinary precautions of laboratory hygiene are necessary when working with this group of organisms

Inter human transmission of undulant fever in Europe has been found negligible with the disease never more than one remove from the goat The same is probably true of the disease in this country of bovine or porcine origin

LABORATORY DIAGNOSIS

The agglutination test used according to the test tube or rapid method is a simple and accurate means of diagnosing the disease in animals A positive reaction in a titer of 1 100 is indicative of active infection A positive reaction in dilutions of 1 25 or 1 50 is considered suspicious Animals reacting in the latter dilutions should be tested again after an interval of 60 days If the reacting titer is higher they should be considered infected

The agglutination test is a highly satisfactory method for diagnosing undulant fever in man in the Island of Malta A positive reaction in a dilution of 1 100 indicates active infection Many cases of the chronic form of the disease in the United States fail to show a positive reaction to the agglutination test For the diagnosis of such cases Huddleson and associates have developed an intradermal allergic test and an opsonic blood test

Allergic tests made intradermally in human beings detect *Brucella* sensitization due to past or present infection A positive test made with any agent does not indicate active infection *Brucella* allergy develops in human beings before the onset of symptoms and may persist many years after recovery

Allergic agents Killed suspension of *Brucella* cells Brucellergen a suspensoid of protein nucleate from *Brucella* cells

Weak suspensions of killed *Brucella* cells have been used and recommended for many years for detecting *Brucella* allergy The

total of 25 polymorphonuclear cells is examined in different sections of the spread and each cell is grouped in one of the four following groups

Negative—When no phagocytosis occurs
Slight—When 1 to 20 bacteria are seen in the cell
Moderate—When from 21 to 40 bacteria are seen in the cell
Marked—When the number of bacteria in the cell is above 40

An individual reacting to the skin test is classified as infected if less than 40 per cent of the cells show marked phagocytosis as questionably infected or immune if 40 to 50 per cent of the cells show marked phagocytosis as immune if 80 per cent or more of the cells show marked phagocytosis If an individual reacts negatively to the skin test and the cells of the blood in a phagocytic system show very little if any phagocytosis such cases are classified as susceptible to Brucella infection

The foregoing interpretation will not apply in many cases of meli tensis infection Very often one observes a high *opsonic* activity in active infection

PREVENTION AND TREATMENT

The protection of the public against infection with undulant fever whether caprine bovine or porcine origin is possible All milk for human consumption should be properly pasteurized Man is not very susceptible to *Brucella abortus* of bovine origin—there fore the fact that the dairy herd is infected with brucellosis is not sufficient cause to reject the milk from such animals for human con sumption A sufficient number of human infections occur however to require the destruction of the organism This is easily accom plished by 30 minutes exposure to a temperature of 142 F

The pasteurization of milk in country districts or on the farm where brucellosis exists among the cattle is more difficult for the process must be carried out on a small scale usually by a busy housewife in addition to a multiple of other duties Boiling may be substituted for pasteurizing The danger of infection is too great to be ignored

The sale of goat s milk should be prohibited where undulant fever is known to exist unless it is pasteurized Man is very susceptible to infection with *Brucella melitensis* Milk from goats shown by test to be free from the disease should be pasteurized as an added pre

3 + = Edema and erythema one centimeter or more in diameter and marked systemic reaction positive

If the clinical symptoms shown by the individual are not sufficiently typical of the disease although a positive intradermal action is obtained the results of the intradermal test should be clarified by performing an opsonic blood test on the patient s blood A satisfactory procedure for performing the test in question and to be used in conjunction with the intradermal test in detecting *Brucella* susceptibility immunity or infection has been worked out at the Michigan State College

Opsonic Test —5 c c of blood are drawn from the patient and placed in 0 2 c c of a 20 per cent sodium citrate solution The blood is shaken thoroughly in order to prevent clotting The specimen should be examined within twelve hours after collection provided it has been kept in a cool place Place in a small test tube 0 1 c c of the citrated whole blood and 0 1 c c of the suspension of a 48 hour growth of a smooth phase strain of *Brucella* in physiological salt solution The density of the suspension should be 1 cm as measured by the Gates apparatus The blood and bacterial suspension are thoroughly mixed and then placed in a water bath 37 C for thirty minutes The cells should be resuspended by shaking after the period of incubation Directly after removing the tubes from the incubator a small amount of the mixture is removed by means of a finely drawn capillary pipette to which is attached a small rubber bulb A drop of the cells is placed at one end of the thoroughly cleaned and polished glass slide and drawn across the slide by placing the end edge of another slide in front of the drop and at such an angle that the spread thins out and terminates at or near the opposite end Blood films should be dried as rapidly as possible to prevent shrinking of the leukocytes Rapid drying may be obtained by placing the slide in front of a small electric fan The slides are stained by covering the spread with 0 5 c c of Hastings stain (Hartman and Leddon Company Philadelphia) After an exposure of 30 seconds 1 c c of distilled water buffered to a pH of 6 is added to the stain on the slide and thoroughly mixed At the end of ten minutes the spread is gently but thoroughly washed free from stain with distilled water and dried in front of an electric fan The *Brucella* opsonic activity of the blood is determined by examining spreads under an oil immersion objective with a 12X ocular A

dous economic importance in animal industry in the United States

8 Protection of the public against undulant fever is easily afforded through proper pasteurization of the milk and by refraining from handling aborted fetuses and fetal membranes and infected animal tissues

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caution Milk from infected goats, when it is necessary to use it should be boiled

For those persons whose occupations expose them to infection such as laboratory workers or employees at abattoirs where hog car casses are handled only eternal vigilance in personal hygiene will protect them

Thus far no treatment has been found which will alter the course of the disease in animals It is known that approximately 12 per cent of cows showing an agglutination titer of 1 500 indicating infection will within one year again become negative to the test Such a change in titer suggests recovery from infection

Numerous biological and chemical agents have been proposed for the treatment of the disease in man The majority of the proposed agents have been used on only a limited number of cases and never under controlled conditions

Huddleson and associates have developed a culture filtrate called Brucellin which has been given an extensive trial on cases in the United States and the Island of Malta It has been studied on cases along with controls in Malta

The results thus show that it reduces the duration of the disease to less than 20 days in 80 per cent of cases The most obstinate cases are those in which the disease has persisted for three months or more before treatment

ITEMS OF NOTE

1 The *abortus suis melitensis* group of organisms is widely dis tributed over the world
2 The common parentage of caprine bovine and porcine strains is indicated by many characteristics
3 *Brucella melitensis* residing long years in the goat as a host has developed virulent properties for man
4 *Brucella abortus* residing long years in the cow as a host infects man at rather seldom intervals
5 *Brucella suis* is very pathogenic for man It is more virulent than abortus strain for all animals
6 Brucellosis of goats is a problem of semi tropical countries Its significance in the United States is relatively small being con fined chiefly to the Mexican border
7 Brucellosis of cattle is a problem of all climates It is of tremen

CHAPTER IV

GLANDLRS*

GLANDERS also known as farcy is primarily a communicable disease of solipeds (horse ass and mule) Secondarily man may become infected through occupational contact with diseased animals or through handling diseased tissues and laboratory cul tures of the causal bacillus

HISTORY

As a disease of the horse and other solipeds glanders appears to have been recognized at a very early period It is mentioned in the writings of Hippocrates between the years 450 B C and 425 B C and by Aristotle a century later From that time the disease has been frequently referred to in veterinary literature

During the fourth century (A D) Apsyrtus and later Vegetius in the fifth century described glanders as being contagious and recom mended the segregation of affected animals Solleysel (stable master to Louis XIV) between 1667 and 1682 expressed the view that it could be transmitted through the air Caspard de Saunier in 1734 regarded the contagion as being conveyed either by direct contact or indirectly through contaminated harness water troughs and feed mangers Viborg in Denmark during the year 1797 published a systematic description of glanders in which he definitely referred to an infectious principle being present in the nasal discharge and the secretions from pustules and ulcers in the skin He likewise considered glanders and farcy to be one and the same disease con tagious in character and transmissible through direct contact and in directly through contaminated feed mangers water troughs harness and stable utensils Unfortunately during the eighteenth and nine teenth centuries conflicting opinions became evident as to the exact

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GLANDERS IN HORSES

Glanders was widely prevalent in most countries until about 1924 when it became noticeably less frequent It still prevails in some parts of Europe Asia and Africa The prevalence and distribution of glanders have always increased during and following all the great wars in different parts of the world —the Civil War in the United States —the British Egyptian War —Afghanistan and South African Wars —the Spanish American War and the World War of 1914 1918 Following the First World War the spread of glanders became intensified in Europe particularly in Russia From the year 1905 a vigorous policy for the control of glanders has been enforced in the United States and Canada with the result that the disease is practically nonexistent in North America

CAUSE AND TRANSMISSION

Glanders is caused by a specific bacterium originally known as *Bacillus mallei* and now designated either as *Malleomyces mallei* or *Pfeifferella mallei* Ordinarily it is spoken of as the glanders bacillus and described as a small slender gram negative rod non spore forming and non motile and growing readily on ordinary culture media The growth on agar has the physical appearance of clover honey on potato media the growth resembles buckwheat honey

In the affected animal the bacillus is present in the nasal discharges and suppurative discharges from the pustules and ulcers (farcy buds) which develop on the skin of the legs and sometimes on other parts of the body as well as in the lungs and the bronchial and submaxillary lymph glands Glanders is chiefly spread through the ordinary channels of horse traffic and the infection can be introduced to the premises through the medium of both clinical and non clinical cases Close cohabitation between the affected and non affected always results in an increasing number becoming infected either in the stable or at pasture Natural infection may occur through the following channels —

1 *By ingestion into the digestive tract* This regarded as the most common mode of infection results from the consumption of feed or water contaminated with nasal discharges

2 *By inoculation through the skin* Slight abrasions of the skin or mucous membrane become infected with the nasal discharges or pustular secretions

origin of glanders One group expressed and supported the view that the disease was of contagious origin while another group vigorously upheld the opposite view

In 1749 Lafosse (senior farrier to the King of France) published A Memoir of the Glanders in Horses in which he described the disease as simple local in character and non contagious The Alfort school of veterinarians in France were at that time strong advocates of the spontaneous origin and non infectiousness of glanders Subsequently however in 1840 Renault and Bouley of Alfort reported that glanders was contagious In England the London school of veterinary surgeons was also divided in its views and as late as 1860 Percival published a comprehensive description of glanders (covering 200 pages) in which he stated No doubt has ever been entertained by me of the spontaneous origin of glanders and farcy—of their origin apart from the influence of contagion He attributed the cause and origin to bad ventilation a miasma, and overcrowding

On the other hand White (1842) published a convincing account of clinical glanders and declared it a contagious disease Likewise Gerlach (1868) and Bollinger (1874) demonstrated that glanders only resulted from direct or indirect contact with an affected animal The definite assertions first made by Viborg in 1797 were ultimately confirmed by the discovery and identification of the causal organism *Bacillus mallei* in 1882 by Loeffler and Schutz in Germany and about the same time by Bouchard Capitan and Charrin in France

An important contribution was made in 1891 when two Russian veterinarians Kalning and Helman and independently Leonard Pearson in the United States produced from pure cultures of the bacillus the product called *Mallein* This product was found to cause a reaction when injected into glandered animals—thus introducing the mallein test as a diagnostic agent for the detection of latent cases The discovery of mallein prepared the way for the ultimate control and eradication of the disease

SUSCEPTIBILITY

Glanders is primarily a disease affecting equines (horse mule and donkey) Man is also susceptible The suppression of glanders in horses results in the disappearance of the disease in man Cattle sheep and swine possess a natural immunity to glanders

Skin lesions Clinical cases are characterized by skin lesions consisting of nodules pustules and ulcers on the skin especially of the hind leg below the hock and on the inner thigh



Ph t by M Gil y

FIG 20—Reactionary edema of the eyelids profuse lacrimation and purulent conjunctivitis following an intradermal injection of mallein into one of the lower eyelids of a glandered horse The so-called intra palpebral mallein test

Respiratory lesions Nodules and ulcers may be present on the surface of the respiratory mucous membrane especially on the nasal septum turbinated bones larynx and trachea

Pulmonary lesions In the majority of cases the lungs are the seat of the disease and are embedded with tubercle like nodules When incised the nodules show a necrotic yellowish centre containing pus Frequently there are definite glanderous pneumonic areas in the lung with suppurating foci discharging into the bronchial tubes

3 *By inhalation into the respiratory tract* While this is possible, it is not considered as the essential or usual mode of infection in animals

SYMPTOMS AND COURSE

Glanders in the horse usually follows a chronic course with a variable period of incubation extending from several weeks to several months The incubation period appears to be relatively shorter in the mule and the donkey Horses kept closely stabled and worked hard develop clinical symptoms in a shorter period than do horses which are kept outdoors on the open range As a result it is customary to speak of two types of the disease (a) *clinical* and (b) *non clinical or latent* glanders

(a) *Clinical cases* are recognized by definite symptoms commonly known as the cardinal signs of glanders" (1) *A chronic* nasal discharge from one or both nostrils with or without visible ulceration of the nasal septum (2) Chronic enlargement and induration of the submaxillary lymph glands on the side of the lower jaw corresponding to the nasal discharge and usually without outward suppuration (3) The presence of pustules and ulcers (farcy buds) on the skin of the legs and sometimes on other parts of the body

(b) *Non clinical or latent cases* are essentially pulmonary in type and the lesions remain in a concealed state in the lungs in the form of tubercle like nodules and suppurating foci In many of these latent cases the affected animal shows only slight signs of chronic lung trouble (altered thoracic breathing) but may spread the infection through respiratory secretions for a period of several months before showing recognizable symptoms These cases are actually more numerous than clinical cases and can be detected only by the application of the mallein test

POSTMORTEM APPEARANCES

Cases of glanders can be diagnosed by means of the mallein test, and a post mortem examination is not always necessary or even desirable, except when performed by a skilled person using proper precautions, owing to the extreme danger of infection while making an autopsy under field conditions The post mortem appearances depend on the nature of the case and comprise one or more of the following gross lesions

Skin lesions Clinical cases are characterized by skin lesions con sisting of nodules pustules and ulcers on the skin especially of the hind leg below the hock and on the inner thigh



Ph t by M GU y

FIG 20 —Reactionary edema of the eyelids profuse lacrimation and purulent conjunctivitis following an intradermal injection of mallein into one of the lower eyelids of a glandered horse The so called intra palpebral mallein test

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Lymphatic lesions The submaxillary lymph gland is frequently found to be enlarged and indurated and while it seldom forms an abscess it may on cross section be found to contain a small amount of caseous pus like material The bronchial and inguinal glands may be similarly affected

Other lesions Lesions may be found occasionally in some of the other organs—the liver spleen and kidney

DIFFERENTIAL DIAGNOSIS

Glanders should be differentiated from such diseases as are characterized by nasal discharge and ulceration of the legs namely dental caries strangles purpura lymphangitis

Dental caries with pus in the facial sinuses In these cases the nasal discharge is quite profuse more so than in glanders and has an offensive odor The nasal discharge in glanders has very little odor The mallein test can be applied where the diagnosis is doubtful

Strangles This is essentially an acute febrile respiratory disease of young horses characterized by profuse nasal discharge and by the development of an acute diffuse painful suppurative swelling in the inter maxillary space Irregular or atypical cases in which the course of the disease is protracted are the most likely to be mistaken for glanders

Purpura haemorrhagica This disease may be clinically distinguished from glanders by the presence of petechiae on the nasal mucous membrane and conjunctiva together with the characteristic edematous swellings on the body and legs

Lymphangitis All forms of lymphangitis accompanied by ulceration of the legs should be differentiated from glanders by means of the mallein test

THE POSITIVE DIAGNOSIS OF GLANDERS

While glanders may be diagnosed by the presence of clinical symptoms the use of the mallein test is essential for the detection of latent cases and as an aid in the routine diagnosis of doubtful or suspected cases There are three recognised methods of applying the mallein test

The subcutaneous mallein test In the application of this test 2 5 c c of dilute mallein are injected subcutaneously into the flat surface of the neck Temperatures are taken before and after the injection

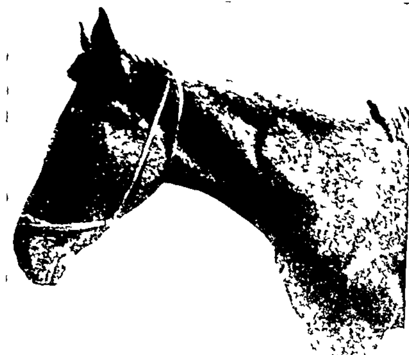
In the glandered horse this test produces in from eight to twelve hours a definite thermal reaction and a distinct painful swelling at the point of injection



FIG 21 —A typical case of cutaneous glanders (farcy) affecting a hind leg

The ophthalmic mallein test In the application of this test the mallein in liquid or tablet form is placed in the fornix of the eye A positive reaction is manifested by the development of a purulent conjunctivitis in the treated eye in from six to twelve hours

The palpebral intradermic mallein test In the application of this test the mallein is injected into the loose fold of skin below the margin of the lower eyelid A positive reaction is manifested by marked swelling of the eyelid accompanied by a pronounced muco purulent secretion from the eye The reaction becomes manifest in from twenty four to forty eight hours



Aft Hutj a a d M r k

FIG 22—The local reaction following an injection of mallein sub cutaneously in the neck of a horse affected with glanders The so called thermic or subcutaneous mallein test

Other methods of test In addition to the foregoing allergic mal lein tests several laboratory methods have been used in the diagno-sis of human glanders and farcy—agglutination precipitin and complement fixation tests and laboratory culture examinations

CONTROL AND ERADICATION

Therapeutic treatment of glanders in horses should not be per mitted as it only leads to further spread and hinders the proper con trol of the disease The only effective policy for the suppression of

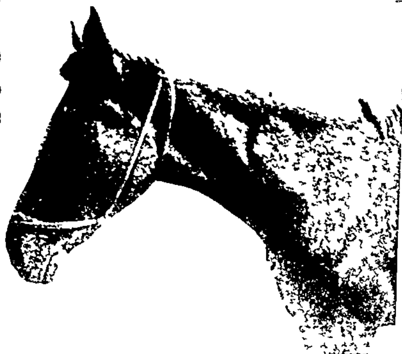


After Hutyra and Marek

FIG 23—Mucopurulent reaction following the instillation of fluid mallein or mallein pellet into the conjunctival sac of a horse affected with glanders So-called ophthalmic mallein test

glanders is compulsory notification and immediate slaughter of all reactors to the mallein test followed by disposal of the carcasses by burial or cremation and the thorough cleansing of the stables and yards Contact horses on the same premises which do not react to the initial test should be held under quarantine pending a retest in two or three weeks Any additional reactors discovered on the retest

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Aft r Huty a a d M k

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have been appallingly high for a time owing to lack of control over the disease in horses

SOURCES OF INFECTION AND TRANSMISSION

Glanders most frequently occurs in man through occupational contact with affected horses or from making an autopsy on a diseased animal and occasionally while making or handling laboratory cultures of *Malleomyces mallei* The majority become infected through abrasions of the skin or mucous membrane—either by the nasal discharge or the secretions from pustules on the skin of an affected animal Transmission of the infection may also take place occasionally if the affected animal coughs or snorts directly in front of the face into the eyes and possibly the nose and mouth Transmission of glanders from one person to another has also been reported as occurring in both men and women while attending and nursing others having the disease This is most likely to occur when the exact nature of the disease has not been recognized and when proper precautions are not taken to prevent infection

SYMPTOMS AND COURSE

The period of incubation in the majority of cases averages from one to five days Cases have been reported in which the incubation period could not be determined exactly and was considered to be several months In such instances it would seem reasonable to assume that they were in reality latent cases and should be regarded as such The onset and manifestations of glanders in man follow the same general typical course in most respects Within a few days following infection prodromal constitutional disturbances develop manifested by fever malaise fatigue loss of appetite jaundice nausea headache and rheumatic pains in the legs In another few days definite physical signs begin to develop in the form of an erysipelatous swelling on the face and the limbs or painful nodules and phlegmonous inflammation (cellulitis) The nodular eruption increases rapidly and soon is followed by a general pustular eruption on the skin over the face and on the legs arms and other parts of the body There is also nasal involvement in which the nasal mucosa becomes reddened and swollen followed by a muco purulent viscous discharge from the nose The nasal discharge is sometimes streaked with blood and associated with ulceration of the nasal septum and other parts of the nasal structures Lymphatic in

should likewise be slaughtered Other contact or exposed horses must be traced and tested to prevent new outbreaks Under this policy of compulsory notification test and slaughter glanders has been effectively controlled and eradicated in the United States Great Britain and Canada In some parts of Europe Asia and Africa where it has not been so dealt with the disease may still prevail

GLANDERS IN MAN

While glanders as a disease of the horse appears to have been recognized and referred to from a very early period (by Hippocrates) no specific description of it as a disease of man is definitely recorded until the early part of the last century This is known as the Travers case reported during the year 1830 and relates to a veterinary student who became infected while dissecting a glandered donkey in London From that time cases of glanders in man began to attract more attention and many authentic cases have since been reported in medical and veterinary literature William Hunting Chief Veterinary Inspector to the London County Council published in 1908 a *comprehensive treatise on glanders in the horse He also included* an appendix relating to glanders in man describing ten cases which he knew to have occurred between 1903 and 1905 A comprehensive monograph A Study of Chronic Glanders in Man was published in *May 1906 by G D Robins M D* of the Royal Victoria *Hospital* Montreal In his treatise Robins reports 156 cases collected from the literature available at that time Bollinger also published an account covering 120 cases In Manitoba two cases were observed and described by McGilvray in *1905* and *1906* There is also the *well known* Gaiger case S H Gaiger a veterinary pathologist at the Punjab Veterinary College became infected while making an examination of a glandered horse He suffered from the disease for a period of nearly two years and underwent 45 operations including the amputation of an arm After recovering he published a graphic account of his illness and sufferings

The Health Department in the City of New York reported 406 cases occurring in the five year period *from 1920 to 1924* The control of glanders in the horse population resulted in a rapid decrease in the disease among the human population This is strikingly illustrated by comparing the vital statistics for New York before and after the year 1924 In 1918 following the conclusion of *the first* World War the incidence of human glanders in Russia is said to

descrıbed as an ıntensely paınful and loathsome dısease from which few recover

DIAGNOSIS

When glanders ıs suspected enquıry should be made to find out whether the patıent had possıble contact wıth glandered horses or a case of human glanders had made an autopsy of a dıseased horse or examıned dıseased tıssues or had undertaken laboratory experı ments wıth cultures of *Malleomyces mallei*

Glanders may be mıstaken for the followıng dıseases and wrongly dıagnosed

Durıng the prodromal stage typhoıd fever rheumatısm jaundıce

Durıng the various stages of pustular eruptıon smallpox tubercu losıs syphılıs erysıpelas lymphangıtıs pyemıa yaws melıoıdosıs

The followıng methods of test may be used for the dıagnosıs of glanders ın man

Blood serum tests The complement fixatıon test the precıpıtın test the agglutınatıon test

Cultural methods A bacterıologıcal examınatıon may be made of the suspected pus and cultures made for the ısolatıon of *Mal leomyces mallei*

Anımal ınoculatıon Male guınea pıgs ınoculated ıntraperıtoneally wıth the pus from a case of glanders frequently develop an acute swellıng of the testıcles and tunıca vagınalıs ın two or three days Thıs ıs known as the Straus guınea pıg test

THERAPEUTIC AND SURGICAL TREATMENT

The medıcınal treatment of glanders ın man has ıncluded the use of many drugs largely tonıc and pallıatıve such as strychnıne quınıne ıron potassıum ıodıde ammonıum carbonate sodıum ben zoate sulphur ıodıne mercurıal and arsenıcal preparatıons Surgı cal treatment ıs necessary ın the majorıty of cases Muscular ab scesses should be swabbed wıth zınc chlorıde and freely opened up to provıde draınage Ulcers and other dıseased focı should be cau terızed eıther wıth the thermocautery or wıth a strong solutıon of carbolıc acıd Where there ıs nasal ınvolvement the nasal passages may be ırrıgated wıth solutıons of potassıum permanganate borıc acıd or sulphanılamıde or by ınsufflatıon wıth ıodoform or arıstol In selected cases the use of sulphonamıdes and antı bıotıc agents sımılar to penıcıllın mıght be further explored—no relıable data have

volvement is also common in the course of which the cervical sub maxillary axillary and inguinal glands may become swollen The final stage of the disease is that of a severe pyemia characterized by the appearance of suppurating pustules covering the body intra



Fig 24 —The pustular manifestation on the arms of a human case of generalized glanders

muscular abscesses metastatic pneumonia diarrhoea emaciation and fatal collapse These symptoms characterize the typical course of acute glanders in man lasting usually from two to four weeks In latent or chronic cases the symptoms are quite similar in character but are prolonged over a greater length of time extending to months and occasionally several years in the form of a pyemia from which a few have ultimately recovered Glanders in man may be tersely

4 The disease in man occurs usually through occupational contact with horses

5 Control and prevention in man depends largely upon eradication of glanders in horses

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been brought forward at the date of this publication Phlegmonous swellings of the face arms and legs may be benefited by the application of saturated solutions of magnesium sulphate or packs saturated with Dakin s solution Biological treatment also offers possibilities through the use of autogenous vaccines and immune sera Watson and others have reported favourable results in several cases following the use of serum from hyperimmunized horses The use of immune serum is deserving of special mention as being of some curative value

PREVENTION AND CONTROL

The prevention of glanders in man is concomitant with the control of the disease in horses Where glanders is suspected among horses those in charge should report such cases to be dealt with under the regulations for the control of contagious disease which require compulsory notification mallein testing and the slaughter of reactors Attendants in charge of affected horses should be warned against the careless handling of horses showing a chronic nasal discharge or an eruption of pustules and ulcers on the skin particularly the legs Laboratory workers should exercise proper precautions in handling diseased tissues and in experimenting with laboratory cultures of *Malleomyces mallei* The bacillus in pure culture should be regarded as highly infectious since a considerable number of laboratory workers have contracted glanders infection In cases of human glanders attendants should take every precaution while feeding handling and dressing the patient and in the proper disinfection and sterilization of instruments bandages garments bedclothes and table utensils It is worth repeating that the prevention of glanders in man depends essentially on the eradication of the disease in horses by the application of the mallein test and the immediate slaughter of all reactors By this method of control glanders is no longer a prevalent disease of animals and man in North America—a striking accomplishment in the suppression of a disease transmitted from animals to man

ITEMS OF NOTE

1 Glanders is primarily a disease of the horse ass and mule
2 The disease was widely prevalent in most countries until about 1924
3 It has been eradicated in the United States and Canada by destruction of infected animals

In the United States the existence of the disease had been suspected for many years As early as 1885 Smith (12) isolated from hogs dead of hog cholera the closely allied mouse septicemia organism which has been confused with the swine erysipelas organism Other investigators had similar experiences In 1920 Ten Broeck (3) found organisms of this group in pigs dead of hog cholera but failed to differentiate between the two species It was generally believed therefore that swine erysipelas did not exist in the United States In 1921 Creech (2) definitely established the fact that the disease did exist in the United States by isolating *Erysipelothrix rhusiopathiae* from several hogs which showed typical symptoms of "diamond skin disease" Klauder (13) in 1926 again called attention to the disease In 1930 there was an outbreak in South Dakota since when swine erysipelas has been receiving more and more attention

THE ETIOLOGIC AGENT

Erysipelothrix rhusiopathiae (*Bacillus erysipelatous suis Bacillus rhusiopathiae suis*) is classified by Bergey (24) among the higher bacteria of the order of actinomycetales The organism is 0 2 to 0 4 microns wide by 1 to 1 5 microns long appears as a straight or slightly curved rod It is not motile and does not form spores It is easily cultivated on the ordinary laboratory media aerobically as well as anaerobically and is gram positive Long threadlike forms may be seen in old cultures

While the organism is destroyed quickly by boiling water and within a few minutes by the usual disinfectants it is very resistant to drying in which state it will remain alive in the dark for a month or more and in the sunlight for 10 to 12 days In salted or pickled meats it will remain alive for 3 or 4 months and in putrid material it is capable of retaining its viability and virulence for months

The organism is widely disseminated its habitat being dead matter of plant or animal origin In certain environments it exists in the soil as a saprophyte or as a virulent pathogen These qualities are not stable since *Erysipelothrix rhusiopathiae* may alternately be virulent or avirulent In addition to this source of infection infection carriers may be found among healthy hogs in erysipelas territory The organism has been recovered from the slime of fish (25) from house flies (26) and from putrefying horseflesh (26) *Erysipelothrix rhusiopathiae* is not the cause of any known disease of fish A more likely explanation of fish source of human infection is the apparent

CHAPTER V

SWINE ERYSIPELAS*

SWINE erysipelas is a communicable disease of hogs caused by *Erysipelothrix rhusiopathiae* man is susceptible to the disease and may be affected through skin abrasions

HISTORY

Swine erysipelas probably has existed in Europe for many years but it was confused with hog cholera and its history is not clear It is said that it was first differentiated as a specific disease in France about 1846 Cartwright in England in 1847 described its chronic form without knowing its true nature Baker in 1873 published in St Bartholomew s Hospital Reports an accurate clinical picture of the disease in man Pasteur in 1883 developed a vaccine for immunizing purposes by passing the organism through rabbits and then making broth cultures Loeffler (11) in 1882 isolated the causative agent of the disease which he designated as Bacillus des Schweine rotlaufs Rosenbach in Germany in 1884 contributed much to the clinical and bacteriologic knowledge of the disease hence the name for the infection in man Rosenbach s erysipeloid Bang in 1888 and McFadyean in 1891 found the organism in chronic heart lesions of hogs

PREVALENCE

The disease is prevalent in Europe where it is known as rouget in France rotlauf in Germany and erysipelas in England It exists to a considerable extent likewise in Austria Denmark Russia Hungary and other countries In England in 1905 in a small strip of country four miles long by one mile broad the disease attacked most of the hogs with 80 per cent mortality (1)

* Prepared by Joseph A Klauder M D Graduate School of Medicine University of Pennsylvania Philadelphia Pa

inson (23) observed that a swollen turgid purplish red caruncle was the most pathognomonic symptom of naturally occurring *Ery sipelothrix rhusiopathiae* infection in turkeys Stiles (35) isolated *Erysipelothrix rhusiopathiae* from a brown rat caught on a dump near a stockyard

The disease in hogs occurs mostly in animals four to eight months old young pigs under three months of age are fairly resistant as are also old hogs This is only a relative immunity however and such animals become infected on some occasions



FIG 25 —Irregular shaped patches of erythema in the septicemic from of *Ery rhusiopathiae* in fection (supplied by L Van Es Department of Animal Pathology University of Nebraska Lin coln Neb)

The infection in swine is manifested in three forms a severe or *septicemic form characterized by constitutional symptoms of septi* cemia presence of diffuse areas of erythema and at times vesicles petechiae and necrosis a mild form (urticarial form or diamond skin disease) characterized by mild constitutional symptoms and presence of sharply circumscribed quadrangular lesions on the skin and a chronic form characterized by polyarthritis and at times by symptoms referable to a vegetative type of endocarditis

Septicemic Form —In the septicemic form the eruption appears on or about the second or third day of sickness The animal is obvi ously sick with high fever Irregularly shaped patches of erythema (fig 25) appear favoring the following regions ears snout axillas lower surfaces of the thorax and abdomen inner surfaces of the thighs groins and perianal region The surfaces of the erythematous patches may be studded with vesicles The involved areas are not tender and the erythema disappears on pressure At the onset the color is pink or light red later it is bright red dark red or purple The purple color compares with the characteristic purple of the

attraction of slime for the organism from refuse thrown in the water and other decaying matter, and that change of environment increases the virulence

Three strains of *Erysipelothrix rhusiopathiae*—the human the swine and the mouse have been reported all probably being variants of a common strain if not identical

When the swine erysipelas organism is injected immediately after isolation it is sometimes but not always virulent for hogs when it has been grown on artificial culture media for any length of time or after it has been passed through some of the experimental animals it loses its virulence and fails to cause disease when injected into pigs Kolda (6) found that when pure bile was used as a culture medium the virulence of *Erysipelothrix rhusiopathiae* was not decreased over a series of transplants but when bile was mixed with other culture ingredients the virulence diminished The virulence is increased by passage through pigeons and decreased by passage through rabbits

THE DISEASE IN ANIMALS

The disease is essentially an affection of swine The white mouse and the pigeon are very susceptible to artificial injection dying within three to five days the rabbit is susceptible to experimental inoculation requiring a large amount of virulent culture intravenously to kill it the guinea pig and the field mouse are immune as are cattle dogs and cats The horse is supposed to be immune but there have been reports of human infection among veterinary students dissecting a horse (17) Christiansen (7) reported an epidemic with high mortality among lambs due to this organism At the time of the outbreak there were no sick hogs in the vicinity Poels found the organism in erysipelas of sheep Schipp (8) in 1910 isolated from chickens suffering from enteritis organisms which could not be distinguished from the swine erysipelas bacillus Broll in 1911 recorded an outbreak in which all the fowls in one flock succumbed within a few weeks to this organism

Pfaff (9) found chickens two to three months old fairly resistant in infection but in chickens one to three weeks old the rotlauf bacillus in pure culture caused an epidemic lasting two to five weeks Jarosch described the organism as the cause of the disease in turkeys and Poels in the pigeon and fowl Beaudette and Hudson (20) have described epidemics of the disease in turkeys Rosenwald and Dick



Fig 27—A swollen turgid purplish red caruncle is the most pathognomonic symptom of naturally occurring *Erysipelothrix rhusiopathiae* infection in turkeys (supplied by A S Rosenwald and E M Dickinson)

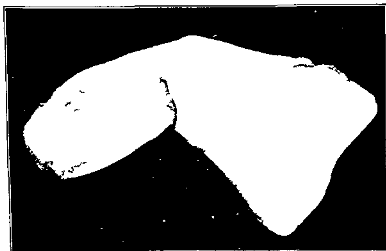


Fig 28—Rhomboidal lesion which gives rise to the name "diamond skin disease" (Klauder)

are raised variously shaped and slightly edematous Other early lesions are spots and ill defined blotches The color in the early eruptive stage is bright red or pink later becoming dark red purplish red and brownish red in the regressing stage The shade of red of some lesions is not uniform throughout Klauder has observed the center to be darker than the periphery Apparently through central clearing extension and joining of lesions a pattern is produced the

localized cutaneous form of infection (erysipeloid of Rosenbach) in man In swine *the lesions which are ill defined may remain local*ized but more likely they enlarge and become confluent affecting the greater part of the cutaneous surface In some cases the erythematous eruption is followed by an outbreak or petechiae As a complication localized or extensive areas of necrosis—a dry form of gangrene—appear in which event the dead skin is stiff and leather like and later is sequestrated This process may involve the entire back The ears and tail may be lost through necrosis If the animal does not die of sepsis or other complication necrotic areas become cicatrized

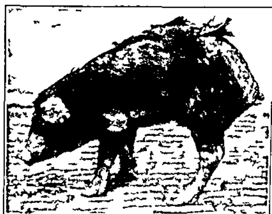


Fig 26 —Sequestration of skin tail and part of ear after necrosis following septicemic form of infection (from G L Dunlap and R Graham Swine Erysipelas Circular 471 University of Illinois College of Agriculture 1937)

Moussu (22) mentioned the occurrence of a hematoma like swelling of the ears violaceous in color which undergoes necrosis

Mild or Urticarial Form ("Diamond Skin Disease) —The eruption in this form is unlike that in the severe or septicemic form *Constitutional symptoms are mild and according to Van Es and* McGrath (24) rapidly improve after the appearance of the eruption Cutaneous lesions may go unnoticed until the animal is slaughtered scalded and cleaned The eruption is characterized by the appearance of a few to a hundred or more variously shaped lesions that may form bizarre designs The eruption is generally described as consisting of raised wheals Wheals are early lesions which through central clearing and peripheral extension form irregularly shaped macules which regress and leave scaly *borders The wheals*

are artificial in appearance as though produced by a brand or as if stuck on the skin

The final stage of the eruption may be presented as desquamation usually at the periphery and as dark brown adherent crusts

Chronic Form —The chronic form usually is subsequent to a previous mild attack of the disease and is characterized by polyarthritis There is first noticed an increased respiration with sometimes a cough followed in a day or two by discoloration beginning at the tops of the ears and spreading along the ventral surface of the body Death results in one to two weeks

Infection is spread from hog to hog directly by ingestion A considerable number of animals may be carriers harboring the organisms either in the intestinal tract or throat Ten Broeck (3) isolated such bacilli from the tonsils of five out of sixteen pigs examined Other workers in Europe previously had had similar experiences Bauermeister in 1901 isolated the organism from the tonsils of 5 normal hogs out of 16 examined Van Velzen in 1907 found it in the tonsils of 3 out of 11 pigs examined Pitt (10) found it in 56 per cent of tonsils of 50 hogs and in 40 per cent of glands of the ileocecal valve of 66 hogs

THE DISEASE IN MAN

Swine erysipelas is conveyed to man through abrasions of the skin invariably the hand resulting in a local infection called erysipeloid of Rosenbach (fig 30) After an incubation period of one to three days pain swelling and erythema appear at site of inoculation A distinctive feature of the erythema is its purplish red color its sharply defined and slightly raised border The erythema slowly progresses involving by continuity adjacent regions or new red patches appear at remote areas The disease may disappear at the areas first involved at the time other areas are affected The affected area is tense and swollen Subjectively there is pain burning and itching sensations which may prevent sleep Mild constitutional symptoms with fever lymphangitis and adenitis may accompany the disease at its onset Stiffness of the joints of the involved finger is another common symptom —at times of adjacent joints indeed the wrist elbow and shoulder These arthritic symptoms may persist for weeks or months after the affected skin becomes normal

Erysipeloid of Rosenbach is frequently confused with pyogenic infection however suppuration never occurs The disease disap

conformation of which is remarkable and unique among diseases of the skin both in man and in animals Although the disease is called diamond skin disease rhomboidal configuration is not always conspicuous and at times is absent Quadrangular, rectangular and ob

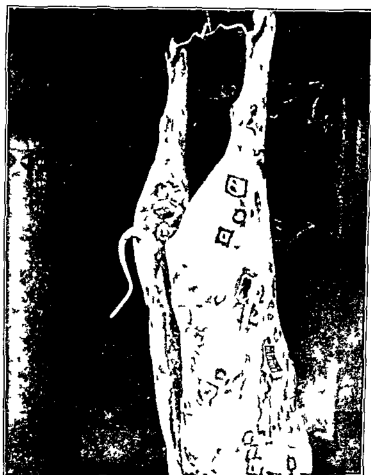


Fig 29 —Picture showing various shaped lesions peculiar to the mild form of infection or diamond skin" disease (Klauder)

long lesions are common and may join in such manner to form a steplike pattern The bizarre designs that the eruption may present sometimes show square lesions containing a smaller square concentrically or eccentrically placed and circinate oval or square lesions with a central discoid lesion (bull s eye)

The lesions vary from about 2 to about 8 cm in diameter They

Kramer and Nicholas (31) described the incident of a butcher who cut his finger on a bone Local infection (erysipeloid of Rosenbach) ensued with bone necrosis Four months after injury he had constitutional symptoms of sepsis an eruption of purpuric macules severe anemia leukopenia with monocytosis Antemortem blood culture revealed *Erysipelothrix rhusiopathiae* Necropsy disclosed vegetative endocarditis in the sections of which *Erysipelothrix rhusiopathiae* was demonstrated

The patient reported by Fiessinger and Brouet (29) became ill after eating salt pork He had an eruption described as red spots on the trunk and extremities A distinctive feature was the swollen purplish red state of both ears comparable to the occurrence at times of a hematoma like swelling of the ears of swine in the acute infection and the swollen caruncle of turkeys There was severe anemia and leukopenia with monocytes Blood culture revealed *Erysipelothrix rhusiopathiae*

Smith (4) reported 6 cases in men all of whom had recently slaughtered infected hogs Linser (5) described a case in a butcher who injured his hand while slaughtering a hog Injection of 25 c c of swine erysipelas serum affected a cure in 3 days Ruprecht states that the disease in man is quite prevalent in lower Bavaria Gerlach in 1925 published an extensive article on the disease in man stating that practically all cases came from contact with swine Bedford and Leeds (15) reported 12 human cases in England all of which occurred in persons 18 years of age or over The lesion in every instance was on the thumb or finger and infection occurred through an abrasion of the skin The sources of infection were fish 5 cases rabbit 2 cases slaughterhouse material 2 cases bird 1 case and unknown 2 cases Stuart (16) in England isolated the organism from a human case

In the United States Klauder has reported many human cases He found in 1932 that the disease was widespread in fishermen along the Atlantic Coast from Maine to Florida The affliction is called fish poisoning because wherever there is an abrasion of the skin infection is almost certain (14) It is thought that possibly the organisms are already on the hands and other parts of the body from the mud and slime in which the fishermen work and that the abrasion makes infection possible Reports from the United States Bureau of Fisheries would indicate that there was no disease of fish

pears without desquamation Extension above the wrist is unusual the average duration is about three weeks

Klauder (27) and others have reported patients who had diffuse or generalized cutaneous eruption with arthritic and constitutional symptoms and negative blood culture

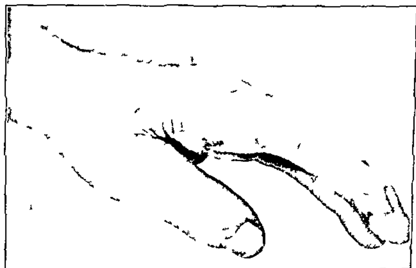


Fig 30 —Human infection with the organism of swine erysipelas

Infection by ingestion through food or water sometimes occurs Habersang (28) reported the case of a butcher who had eaten freely of raw sausage made from the flesh of hogs that were subjected to emergency slaughter on account of septicemic form of *Erysipelothrix rhusiopathiae* infection The patient had constitutional symptoms and a generalized eruption which was attributed to *Erysipelothrix rhusiopathiae* infection Recovery ensued There was no history of wound infection Gastrointestinal source of infection seemed likely In the case reported by Fiessinger and Brouet infection occurred from eating salt pork (29)

A few cases of septicemic form of infection in man have been reported Russell and Lamb (30) described the case of a lobster fisherman who presented a hospital course of sepsis with endocarditis Death occurred after three months illness Antemortem blood culture revealed *Erysipelothrix rhusiopathiae* Vegetative endocarditis of the aortic and mitral valves were found at autopsy Klauder,

istered the second of which was more virulent than the first Sometimes however such living virus initiated the disease in healthy animals The method has been modified therefore so that immune serum is given to the animal at the same time that the living culture is given Immune serum is likewise efficacious in curing the disease if it is given early

The prevention of the disease in man depends upon painstaking care by those persons who come into contact with infected hogs and by fishermen and others handling dead animal matter that abrasions of the skin do not become contaminated

ITEMS OF NOTE

1 Swine erysipelas is primarily a disease of hogs and poultry
2 Few other animals are susceptible to infection
3 The causative organism is widely disseminated its habitat being dead matter of plant or animal origin
4 Man is infected through abrasions of the skin and rarely by ingestion
5 The prevention of the disease in hogs may be accomplished by vaccination plus immune serum
6 The prevention of the disease in man requires precaution as to cuts and abrasions by those who come into contact with hogs and by fishermen and others handling dead animal matter

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known which is caused by the bacillus of swine erysipelas Fisher men in fresh waters are less subject to the disease but infection from this source does occur

Table 15 —Sources of Infection or Occupation of 100 Patients with Erysipeloid

Abattoir	58
Fish retail	11
Tallow grease fertilizer	7
Veterinary student (dissecting horse)	6
Butchers retail	3
Fishermen pleasure	3
Bakers (lard)	2
Clam opener	1
Food handler	1
Furrier (unfinished pelt)	1
Rabbit (removing skin)	1
Opossum (carrying animal)	1
Weaver	1
Dressmaker	1
Housewife (cleaning fish)	1
Fish (handling)	1
Kitchen worker	1

Klauder (17) has reported on 100 cases occurring in the United States with particular reference to the occupational nature of the disease Eighty eight cases were infected through injury to the hands in the ordinary course of employment The source of infection is given in table 15

Reports of many other cases are appearing Lawson (14) en countered an epidemic of 210 cases among employees of a button factory where cattle bones were utilized It is said that about 2 per cent of employees in an abattoir in Philadelphia are infected annu ally

Treatment of swine erysipelas by the sulfonamides in mice was found not to be effective by Porter and Hale (32) The use of sul fonamide compounds both by mouth and locally was without value in human infections according to Klauder and Rule (33) Heilman and Herrell (34) observed the use of penicillin in mice the mortality rate was 100 per cent in untreated mice and 5 per cent in treated animals It would seem that penicillin is also effective in human in fections

PREVENTION

The prevention of swine erysipelas in hogs can be accomplished by vaccination Pasteur originally used living organisms attenuated by passage through rabbits two doses of the material being admin

CHAPTER VI

SALMONELLA FOOD INFECTIONS

SALMONELLA food infections are caused by one or another of the *Salmonella* bacteria of which more than a hundred types have been reported Many of these have been found in animals or birds and the types which cause gastro enteritis in man are constantly increasing in number

HISTORY

Food infection is as old as civilization itself From his earliest creation down through the ages man apparently acquired considerable knowledge concerning what was good to eat and what to let alone By the fourth century B C it was recognized that the bodies of animals dying a natural death were not fit for food for Moses commanded that Ye shall not eat anything that dieth of itself Moses was not particularly concerned about the ethics of the matter however for he permitted that Thou mayest give it unto the sojourner within thy gates that he may eat it or thou mayest sell it unto a foreigner (2)

Food poisoning mentioned by Hippocrates Horace Ovid and other ancient writers was often of a different nature usually having to do with poisonous mushrooms or other poisonous foods Later conceptions of food poisoning were purely chemical in nature With the advent of bacteriology the term ptomain came into common use to cover all forms of food poisoning The wide newspaper publicity of every case of botulism that occurred placed an undue emphasis upon this form of food poisoning in the minds of many persons so that the term botulism and food poisoning were synonymous whatever the cause Many food poisoning outbreaks were without doubt due to staphylococcus but it was not until about 1930 that they were recognized

Salmon and Smith in 1885 isolated *Salmonella choleraesuis* (B

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Due to the above reasons we have no accurate knowledge concerning the prevalence of bacterial food poisoning There are probably thousands of unreported and uninvestigated outbreaks each year

THE ETIOLOGIC AGENTS

Salmonella organisms are small gram negative non spore forming motile rods which grow well on culture media and ferment many sugars with acid and gas (with some exceptions)

They have been variously known as the paratyphoid group the Gaertner group the hog cholera group the enteritidis group the intermediate group and the Salmonella group More than a hundred types of the germs have been isolated and classified into different groups on a biochemical and serologic basis A classification on the basis of host susceptibility is not possible at the present time

New types are being discovered with the progress of years and are being added to the different groups It has been customary to name a new type after the place where the organism was first isolated Some of the Salmonella types which have caused gastroenteritis in man and which have been found in healthy or diseased animals are listed in table 16 Many of the types have been encountered but a few times Bornstein (4) considers all types of Salmonella pathogenic for man although all have not yet been isolated from human sources

The typhoid bacillus *Eberthella typhosa* is related to the Salmonella organisms serologically falling into group D While it is classified with Salmonella (*Salmonella typhi*) by some authorities in the United States Bergey does not include it It is rarely found in animals (one instance) *S paratyphi* A (the paratyphoid A bacillus) is included in group A and *S paratyphi* B (the paratyphoid B bacillus) is in group B The occasions when they have been found in animals are exceptional

Salmonella organisms grow rapidly in most foodstuffs without producing much evidence of their existence Koser (17) found that all types multiplied rapidly in the liquor of several cooked vegetables with the exception of highly acid sauerkraut In fruit juices a rapid destruction of the organisms took place In several meat products the organisms exhibited a marked ability to spread from the original point of inoculation throughout the foodstuff although this occurred only under optimum conditions Damon and Leiter (18)

cholerae suum Bact suipestifer the hog cholera bacillus) from hogs suffering from cholera which was thought to be the cause of the disease It was the first organism of the group to be described hence by priority the term Salmonella

Gaertner in 1889 reported the illness of 57 persons who had eaten the flesh of a cow that had been killed because it was sick One man who consumed nearly two pounds of the raw meat died in thirty five hours From the organs of the man as well as from the meat he had eaten Gaertner isolated the causative agent *Salmonella enteritidis* (*B enteritidis* the Gaertber bacillus)

DeNoble in 1889 isolated *Salmonella typhimurium* (*S aertrycke B aertrycke B pestis cavae*, the mouse typhoid bacillus) from a food poisoning outbreak

Much confusion has existed in the identification and nomenclature of Salmonella organisms Different names have been applied to the same organism isolated in different countries or the same name has been used to describe different organisms It was many years before Salmonella typing centers were established and accurate identification made available

PREVALENCE

Accurate figures concerning the prevalence of food infection in the United States are lacking compulsory reports of such instances are not required many of the reports taken from the daily press are wholly unfounded and few of the actual outbreaks are carefully studied

Statistics regarding the causative agents in outbreaks of food poisoning are usually inaccurate Food samples submitted for investigation are often unsatisfactory having been stored improperly or too long before culturing Undoubtedly only a small number of cases of food infection which occur in family groups are reported whereas when large gatherings of people are afflicted the attention of the public is called to the episode This is due to the fact that the symptoms may be mild or if severe of short duration Previous to 1930 laboratory workers investigating the causative agents of food poisoning outbreaks were concerned principally with Salmonella or *Clostridium botulinum* and they overlooked those outbreaks due to staphylococci Even now the assay of the staphylococcus isolated is difficult and staphylococci are often reported as the causative organism without adequate evidence

ANIMALS AND BIRDS RESPONSIBLE FOR FOOD INFECTIONS

Poultry —Poultry and other birds have caused many cases of Sal monella food poisoning Barnes (37) considers the domestic fowl as the main animal reservoir of organisms affecting man He lists 20 types of Salmonella in which the domestic fowl is the chief reser voir (table 17)

The hen is commonly infected with S *pullorum* which is trans mitted to the egg Human infections have been reported by Mickle and his co workers (16) and by Edwards and Brunner (24) Com mercial egg preparations have been found to contain *S seftenberg* and *S paratyphi B* (33) The duck is infected with several varieties of Salmonella organism and Snapper (28) has reported human out breaks caused by duck eggs Turkeys were found to harbor 23 types of Salmonella (36) among the most common of which were *S pullorum* and *S typhimurium* Turkey eggs harbored the former organism from 8 per cent of the birds examined Goose eggs and pigeon eggs used in the preparation of salads and puddings have caused human Salmonella infections

Swine —Hogs have been found to harbor many types of Salmon ella organisms Salmon and Smith considered *S choleraesuis* to be the cause of hog cholera but it has since been shown that it is a secondary invader in hog cholera It is an ordinary inhabitant of the intestinal tracts of hogs to which no significance is attached under normal conditions When the resistance of the animal is low ered it takes on special pathologic significance as a secondary in vader Jordan isolated *S choleraesuis* *S typhisuis* and *S para typhosus B* from the organs of diseased hogs He obtained no Salmonella organisms from the organs of 291 normal swine

Cherry and his co workers in Lexington found 10 samples infected in 170 samples of market pork The organisms were *S typhimurium* *S derby* *S seftenberg* *S anatum* *S bredeney* *S give* *S newing ton* and *S newport* Rubin Scherago and Weaver (27) studied mesenteric lymph glands in a thousand hogs in groups of 25 each There were 242 cultures of Salmonella isolated falling into 13 types Other workers have had similar experiences Savage and White (6) encountered *S enteritidis* twice and *S choleraesuis* once from porcine sources in 31 epidemics of food poisoning which were care fully studied

had a similar experience, finding that under ordinary household conditions the organisms will multiply to a considerable extent in 24 to 72 hours producing such slight changes in color and odor as to be readily overlooked

Table 16—SALMONELLA ORGANISMS WHICH HAVE CAUSED GASTRO-ENTERITIS IN MAN AND WHICH HAVE BEEN ISOLATED FROM ANIMALS FROM BORNSTEIN (4)

GROUP B	
S typhimurium	natural pathogen of animals
S heidelberg	from a pig
S chester	from a normal hog
S san diego	from fowl and swine
S saint paul	from turkeys
S reading	from swine
S derby	from swine fowl and ruminants
S bredeney	from fowl hogs and ruminants
S schleissheim	pathogen for animals
GROUP C 1	
S choleraesuis	pathogen for animal secondary invader in hog cholera
S thompson	from hog and fowl
S montevideo	from various animals
S oranienburg	epizootics in quails and chickens
S braenderup	from a fatal diarrhea
S bareilly	from chicken swine and carnivores
GROUP C 2	
S newport	from various animals
S muenchen	from hogs and other animals
S litchfield	from fowl
S morbificans	from a diseased cow
S glostrup	from a diseased dog
GROUP D	
S enteritidis	pathogen for animals
S dublin	pathogen from animals
S panama	from fowl and swine
GROUP E 1	
S london	found in healthy and diseased animals
S give	found in fowl and swine
S anatum	pathogen for various animals
S malaegridis	found in fowl and swine
GROUP E 2	
S newington	pathogen for fowl found in swine and rodents
S newbrunswick	from fowl hogs and ruminants
GROUP E 3	
S seftenburg	from fowl and swine
GROUP F	
S kentucky	from chicken with enteritis and from camels
S aberdeen	from fowl
S rubislaw	from fowl
S wichita	from swine and turkey
S worthington	from fowl and swine
S hvittingfoss	from animals
S cerro	from hog and fowl
S urbana	from enteritis in a hog and from diseased chicken

ever and several European epidemics have been reported from such animals The famous mutton strain" was isolated from a man in Newcastle in 1911 Several epidemics of disease in sheep as well as food poisoning epidemics in man have been caused by organisms identical with the "mutton type Sheep are of less importance than cattle or hogs in food poisoning Cherry and his co-workers found no Salmonella organisms in eleven samples of market lamb

Rodents—Rodents are extremely susceptible to infection with Salmonella organisms Friesleben (19) found 52 per cent of wild mice and 19 per cent of wild rats carrying such organisms in their intestines Meyer (8) found 58 infected animals among 775 wild rats examined—28 with *S enteritidis* and 30 with *S typhimurium* Zwick and Weichel found 28 out of 177 mice carrying such organisms Verder (9) isolated *S typhimurium* from the spleen of one rat out of 114 examined

Welch Ostrolenk and Bartram (29) examined 420 specimens of rat droppings collected from all regions in the United States Only five showed Salmonella organisms Rat droppings kept at room temperature remained infective for 148 days Transfer of infection from an infected rat or mouse to cage mates did not take place in the experience of these investigators Price Jones (20) fed enteritidis bacilli to rats observing them in the liver and spleen in 48 hours Two months later 10 per cent of the animals were carriers while after five months a few animals still persisted as carriers Such healthy carriers were capable of starting new epidemics among other rats

Guinea pigs have been found infected with *S typhimurium* A few instances of infection in rabbits have been reported Neither guinea pigs nor rabbits are relatively important compared to rats and mice

Other Animals—Other animals harbor organisms of the Salmonella group but their relation to food poisoning is of less significance

The horse has been responsible for several outbreaks of Salmonella food poisoning in Germany through the use of horse meat as a food The horse is commonly infected with *S abortus equi* but human infections are probably rare *S muenster* was isolated from one human case in Germany that consumed raw horse meat

The dog carries *S enteritidis* (21) and *S anatum* (31) as does also the cat (22 23 31) Jordan (12) included in his collection of food poisoning organisms a culture of *S choleraesuis* isolated from

Table 17 —TYPES OF SALMONELLA ORGANISMS LISTED IN ORDER OF FREQUENCY FOUND IN MAN (BARNES 37)

TYPE	HUMAN OUTBREAKS	ANIMAL OUTBREAKS
S paratyphi B	51	Fowls 4 others 2
S typhimurium	50	Fowls 472 others 10ɔ
S newport	33	Fowls 19 others 7
S choleraesuis	30	Swine 272 others 32
S panama	20	Fowls 6 others 1
S montevideo	17	Fowls 11 others 3
S oranienburg	13	Fowls 28
S san diego	13	Fowls 3 others 1
S bareilly	11	Fowls 47 others 7
S anatum	10	Fowls 44 others 12
S enteritidis	8	Rodents 12 others 7
S bredeney	7	Fowls 27 others 6
S give	6	Fowls 18 others 7
S seftenberg	4	Fowls 15 others 4
S meleagridis	3	Fowls 15 others 1
S oregon	3	Swine 5 others 2
S derby	2	Fowls 33 others 9
S saint paul	2	Fowls 1
S thompson	2	Fowls 1
S pullorum	2	Fowls 492 others 3
S newington	2	Fowls 18 others 4

Cattle —Cattle suffer from puerperal fever diarrhea septicemia uterine inflammations and the like caused by Salmonella organisms Gaertner isolated *S enteritidis* from the meat of a cow that had been slaughtered because it was sick McWeeney (7) encountered the same organism in beef stew Savage and White isolated it three times from bovine sources in thirty one food outbreaks It occurs occasionally as an inhabitant of the intestinal tract of cattle

Uhlenhuth reported the occurrence of Salmonella organisms in the intestines of healthy calves and cattle but Jordan's (12) study on the intestinal contents of fifty two normal cattle killed at the Union Stock Yards in Chicago showed no organisms that fulfilled all the requirements of the food poisoning group Friesleben (19) examined the intestinal contents of 100 cattle with similar results

Cherry Scherago and Weaver (26) examined sixty four samples of beef in the markets of Lexington Kentucky and found three which contained Salmonella organisms If the hamburger was ex cluded (which may have contained some pork) there was only one sample in forty that was infected This contained *S seftenberg*

Sutherland and Berger (32) encountered an epidemic among 162 persons in England due to *S dublin* in milk The cow suffered from a gastro enteritis

Sheep —Sheep in health harbor no food poisoning organisms They are subject to infection with *Salmonella typhimurium* how

finding S *typhimurium* in thirty seven per cent Mickle and his co workers (16) encountered it in thirty four per cent of human Salmonella cases Edwards and Bruner (24) found it in seventeen per cent of human cases and in forty seven per cent of Salmonella cultures isolated from animals Seligman (25) found 369 out of a thousand human cases of Salmonella infection due to S *typhimurium* There were nineteen deaths

Outbreaks due to S *choleraesuis* are relatively common (table 17) This type constituted thirteen per cent of Bornstein s cultures of Salmonella from human cases two per cent of Mickle s cultures and eight per cent of Edward s Seligman had ninety cases of choleraesuis infection with sixteen deaths in a thousand Salmonella patients

S *enteritidis* has received much publicity but it is not found as often as many of the other Salmonella organisms Bornstein found it constituted only four per cent of 429 Salmonella cultures from human cases Mickle Edwards and Seligman each had a figure of three per cent In cultures of Salmonella from animals Edwards found it constituted two per cent of the total

ENTERIC FEVER

Enteric fever includes those infections manifested by a continued fever of the enteric type in which there is an early invasion of the blood stream The appearance of symptoms occur usually from seven to fourteen days after ingestion of the organisms Blood cultures are usually positive as soon as symptoms appear Later when the organisms have become localized in the intestinal mucosa stool cultures are positive

Sometimes following bacteremia the organisms locate in regions other than the intestinal muco a Bornstein (4) includes among pathologic conditions thus found endocarditis pericarditis meningitis osteomyelitis arthritis rhinopharyngitis sinusitis pneumonia pleurisy peritonitis cholecystitis pyelonephritis and abscesses

D Albora Ingens and Edson (38) reported nineteen cases of bronchopneumonia following an outbreak of 350 cases of gastro enteritis due to S *montevideo* Other investigators have found that a small percentage of enteric fever and associated infections sometimes follow gastro enteritis due to Salmonella food poisoning

More than thirty types of Salmonella have been implicated in enteric fever (37)

the mesenteric gland of a monkey and a culture of *S typhimurium* isolated from the spleen of a skunk

GASTRO ENTERITIS IN MAN

Salmonella food poisoning in man is an infection rather than an intoxication The incubation period is usually eight to twenty four hours, though sometimes it is a little less and sometimes as long as seventy two hours The onset is sudden with a headache and a chill and often with vomiting Nausea abdominal pains and severe diarrhea are characteristics of the infection The temperature is elevated at first The symptoms rapidly diminish after a few days Mortality *does not exceed one or two per cent of the cases (Table 18)*

Table 18 —Symptoms of Salmonella Food Poisoning Compared With Food Intoxications (after Dack)

Symptoms	Botulism Intoxication	Staphylococcus Intoxication	Salmonella Infection
Incubation Period	Average 1 or 2 days	*1 to 6 hours* Average $2\frac{1}{2}$ to 3 hours	7 to 72 hours
Onset	Gradual	Sudden	Sudden
Vomiting	About $\frac{1}{3}$ of cases	Common	Common
Diarrhea	*Uncommon*	Severe	Severe
Constipation	Common	Absent	Absent
Abdominal pain	Absent	Present	Present
Temperature	Subnormal	Variable	Elevated at first
Prostration	Absent at first	Acute	Present
Nervous System	Double vision difficulty in swallowing in speech and in respiration	Not involved	Not involved
Duration of symptoms	Protracted and progressive Convalescence slow	5 to 6 hours or longer	Rapidly diminishing
Mortality	65 per cent of cases	Practically nil	1 or 2 per cent of cases

The severity of the symptoms vary in different outbreaks possibly depending upon the size of the infecting dose All members of the group however which cause gastro intestinal upsets produce identical symptoms All age groups of people are susceptible to Salmonella infection (33) Among 425 cases of gastro enteritis in Massachusetts caused by these organisms *S typhimurium* was the most common cause Thirty nine per cent of patients infected with *S typhimurium* were under ten years of age These figures are in accord with the findings of Barnes (table 17) as well as others

Bornstein (5) studied 429 Salmonella cultures isolated from man,

free from rodents which may contaminate food directly with droppings Flies and other insects that carry infection mechanically from rat droppings or other dejecta must be prevented access to food supplies Persons who handle pets should wash their hands thoroughly before eating or preparing food The same precautions but perhaps to a lesser extent should be observed in regard to human carriers as for other enteric infections

ITEMS OF NOTE

1 There are more than a hundred types of Salmonella organisms many of which cause gastro-enteritis in man
2 The usual period of incubation in Salmonella food poisoning is seven to seventy two hours
3 Enteric fever with infection of the blood stream sometimes follows gastro enteritis Salmonella organisms travel from the blood stream to other parts of the body where they cause a miscellaneous number of disabilities
4 The domestic fowl is apparently the chief reservoir of Salmonella organisms The hog cow sheep or rat are the other animals usually associated with this type of food poisoning
5 *The house fly is a mechanical carrier of Salmonella organisms*
6 Prevention consists in the use of meat products and eggs from healthy animals and birds and in the protection of food supplies from contamination by rats and flies

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EPIDEMIOLOGY

The epidemiology of Salmonella food poisoning is not always clear Meat products from infected animals or poultry are often but not always the cause For instance human infections with S *suipestifer* are rare on farms where hog cholera (with associated suipestifer infection) is common Even consumption of pork from such hogs does not necessarily produce illness The same condition exists in regard to the consumption of poultry and eggs from flocks infected with S *pullorum*

Flies have been implicated as mechanical carriers of Salmonella organisms Gwatkin and Mitchell (30) showed that they carried S *pullorum* from chicken dropping Ostrolenk and Welch (34) also implicated the house fly in the spread of Salmonella organisms, while Braun found that the mosquito *Culex pipiens* was a vector Parker and Steinhaus (35) demonstrated that the wood tick *Dermacentor andersoni* transmitted S *enteritidis* experimentally

Commercial rat viruses usually contain the enteritidis organism several human epidemics are traceable to such products (12) Spray reports an outbreak involving 123 cases due to contamination of milk with a commercial rat virus (13)

Human carriers sometimes are responsible for food poisoning epidemics D Albora Ingens and Edson (38) reported such an outbreak involving 350 cases due to S *montevideo* from a carrier in the kitchen who contaminated rice pudding The carrier state is usually regarded as of rather short duration after infection but it may exist for a considerable time

Rubenstein (33) found that convalescents showed Salmonella organisms in the stools in forty three per cent of 711 cases after the fourth week from onset eighteen per cent after the eighth week and eleven per cent after the tenth week Sixteen cases were permanent carriers none of which were among the S *typhimurium* cases

PREVENTION OF FOOD INFECTIONS

Hogs cattle or sheep which are sick should not be used for food The emergency slaughter of sick animals is not generally practiced in the United States and careful inspection of regularly established abattoirs eliminates many diseased animals Adequate cooking of meat and poultry is a safeguard Eggs should not be eaten raw Foods in markets and bakeries as well as in the home must be kept

CHAPTER VII

LISTERELLOSIS *

LISTERELLOSIS is a specific infectious and often fatal disease of sheep cattle rabbits guinea pigs and chickens In ruminants it is characterized by symptoms involving the central nervous system though in rodents it assumes a septicemic form In chickens the principal lesions are in the myocardium It has also been reported in foxes pigs and goats as well as in man The disease in man is accompanied by disturbances of the central nervous system

HISTORY

Murray Webb and Swann isolated the organism in rabbits and guinea pigs in 1926 in England and gave it the name *Bacterium monocytogenes* because the disease was characterized by an increase in the number of circulating monocytes Recognizing the causative organism of Tiger river disease in rodents to be a new genus Pirie (1927) in South Africa gave it the name *Listerella* and suggested the specific name *hepatolytica* because of the liver lesions it produced When an exchange of cultures showed that the organisms isolated by Pirie and by the workers in England were the same Pirie withdrew the name *hepatolytica* in favor of the earlier name *monocytogenes* After Becker (1939) pointed out that the generic name *Listerella* had already been used for a mycetozoon Pirie (1940) suggested that a new name *Listeria* be used This name however was not adopted because it had already been given to a certain plant group

Listerella was first recognized as a cause of disease in domestic animals by Gill (1931) when he isolated the organism from sheep in New Zealand and gave the name circling disease to the encephalitis which it caused Goodpasture reported the disease in rabbits in

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Table 19 Continued

Host	Observer	Date Report was Published[a]	Place of Origin or Study	Type of Disease
Pig	Pomeroy Fenstermacher and Andberg	1943	Minnesota	Encephalitis
	Slabospits kii	1938	Russia	Pox like
	Biester and Schwarte	1940 41A	Iowa	Encephalitis
Horse	Jones[d]	1940	Virginia	Periodic ophthalmia
Fox	Cromwell Sweebe and Camp	1939	Illinoi	Distemper like
Man	Atkinson	1917	Australia	Meningitis
	Dumont and Cotori	19?1	France	Meningitis
	Baldridge Rohner & Hausmann	1926	United States	Infect mononucleosis
	Nyfeldt	1979 3?	Denmark	Infect mononucleosis
	Tesdal	1934	Norway	Meningitis
	Schultz Terry Brice and Gebhardt	1934 38	California	Meningitis
	Burn	1934 35 36	Connecticut	Meningitis
	Gibson	1935	Scotland	Meningitis
	Allen[f]		Connecticut	Meningitis
	Carey	1936	Massachusetts	Meningitis
	Poston Upchurch and Booth	1937	North Carolina	Meningitis
	Schmidt and Nyfeldt	1938	Denmark	Infect mononucleosis
	Cislaghi	1938	Italy	Meningitis
	Pons and Julianelle	1939	Missouri	Infect mononucleosis
	Porzecanski and de Baygorria	1939	Uruguay	Meningitis and otitis media
	Wright and Macgregor	1939	Scotland	Meningitis
	Wagner and Porter		Iowa	Meningitis
	Savino	1940A B	Argentina	Meningo-encephalitis
	Fischer	1941	Uruguay	Meningo-encephalitis
Chicken	Ten Broeck		New Jersey	Generalized infection
	Paterson	1937 39A	England	Generalized infection
	Watkins[i]		England	Generalized infection
	Pallaske	1940	Germany	Generalized infection
	Cole	1941	New York	Generalized infection
	Hurt Levine and Graham	1941	Illinois	Generalized infection

These reports are listed in the bibliography [b] Did not identify as listerellosis but it probably was this disease Observation reported by Seastone (1935) [d] Relation of this strain of *Listerella* to that isolated by other investigators is not certain Classified organism as a diphtheroid but it may have been *Listerella* [f] Observation reported by Burn (1936) Did not isolate *Listerella* [h] Observation reported by Porter and Hale (1939) [i] Observation reported by Paterson (1939)
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established the avenues of infection and the mode of transmission has not been determined Little progress has been made in immunizing susceptible animals

ETIOLOGY

The causative organism *Listerella monocytogenes* is a Gram positive rod 1 by 0 5 microns (see Fig 31) In hanging drop prepa

Tennessee in 1924 but the relation of this strain of *Listerella* to that isolated by other investigators was not established

To date the causative organism has been isolated in the United States from eight different animal species as well as man and from eight hosts in Germany Uruguay Argentina Scotland Italy, Denmark, Norway France Australia Russia England New Zealand South Africa and Sweden (see Table 19)

Experimental studies on epizoology and immunology have not

Table 19—REPORTS OF SPONTANEOUS LISTERELLOSIS

HOST	OBSERVER	DATE REPORT WAS PUBLISHED	PLACE OF ORIGIN OR STUDY	TYPE OF DISEASE
Rabbit	Goodpasture	1924	Tennessee	Encephalitis
	Murray Webb and Swann	1926	England	Generalized infection
	Paterson	1940C	England	Generalized infection
	Henricson	1943	Sweden	Generalized infection
Guinea pig	Murray Webb, and Swann	1926	England	Generalized infection
Gerbille	Pirie	1927	South Africa	Generalized infection
Sheep	Gill	1931 33 37	New Zealand	Encephalitis
	Doyle[b]	1932	Indiana	Encephalitis
	Ten Broeck		New Jersey	Encephalitis
	Jungherr	1937	Connecticut	Encephalitis
	Graham Dunlap and Brandly	1938	Illinois	Encephalitis
	Morin	1938	Illinois	Encephalitis
	Biester and Schwarte	1939	Iowa	Encephalitis
	Paterson	1939A 40D	England	Abortion
	Graham Hester and Levine	1940B	Illinois	Encephalitis
	Olafson	1940	New York	Encephalitis
	Pallaske	1940	Germany	Encephalomyelitis
	Cross	1941	Colorado	Encephalitis
	Henderson	1941	Illinois	Encephalitis
	Hoffman	1941	California	Encephalitis
	Jensen and Gay	1941	Illinois	Encephalitis
	Muth and Morrill	1942	Oregon	Encephalitis
	Pomeroy Fenstermacher and Andberg	1943	Minnesota	Encephalitis
Goat	Olafson	1940	New York	Encephalitis
	King	*1940*	*New Jersey*	Encephalitis
	Gifford and Eveleth	1942	Arkansas	Encephalitis
Cattle	Mathews[b]	1928	Indiana	Encephalitis
	Jones and Little	1934	New Jersey	Encephalitis
	Fincher[b]	1935	New York	Encephalitis
	Graham Dunlap and Brandly	1938	Illinois	Encephalitis
	Graham Hester and Levine	1939 40A	Illinois	Abortion
	Graham Hester and Levine	1940B	Illinois	Encephalitis
	Biester and Schwarte	*1941B*	Iowa	*Encephalitis*
	Paterson	1941	England	Hepatitis
	Schwarte and Biester	1942	Iowa	Encephalitis
	Evans and Sawyer	1942	Vermont	Abortion

SEASONAL INCIDENCE

Listerellosis in ruminants usually occurs in winter and early spring when animals are confined in feedlots In Illinois New York and other states reported outbreaks have occurred from December through June although one case in dairy cattle in Illinois occurred early in July Although the disease has occurred in sheep that had been on pasture as long as four weeks losses usually subside and the clinical disease disappears after animals are placed on pasture These facts indicate that crowding may favor transmission of the disease Dry feeds during the winter may lower resistance sufficiently to allow the organism to gain a foothold and possibly the lack of some essential nutrient in the ration so alters the defensive mechanism particularly the nasal mucous membrane as to favor infection

EPIZOOTIOLOGY

Sporadic outbreaks reported in different sections of the United States suggest the widespread distribution of this disease but knowledge of the reservoir and the method by which the disease is spread from animal to animal is not known

Gill (1931 1933 1937) suggested that the sheep nasal fly *Oestrus ovis* might be the transmitter of the disease but this has not been confirmed The absence of the larvae in some affected sheep together with the occurrence of the disease in cattle and in spring lambs suggests that other factors may be involved in the transmission

Table 0—LOSSES FROM LISTERELLOSIS IN OUTBREAKS AMONG SHEEP IN ILLINOIS

OUTBREAK No	ANIMALS IN HERD	ANIMALS DEAD		OUTBREAK No	ANIMALS IN HERD	ANIMALS DEAD	
		Number	Per cent			Number	Per cent
1	300	30	10 0	4	180	12	6 7
2	100	8	8 0	5	300	101	33 5
3 (1st year)	800	40	5 0	6	—	—	—
(3d year)	891	5	6 4	7	—	12 15	—
(4th year)	1[illegible]0	46	4 5				

Exclusive of 31 lambs born during the outbreak
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On an Illinois farm an outbreak of ovine listerellosis occurred one winter when there were many rats in the barns The next winter

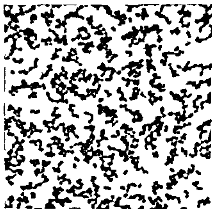


Fig 31—Causative Organism of Listerellosis *Listerella monocytogenes* (magnified 1200 X) *Illinois Agri Exper Sta Bull 499*

rations the species exhibits a rather peculiar tumbling motility that appears to be characteristic All strains isolated at the Illinois Experiment Station are beta hemolytic and grow well at 37°C as well as at room temperature Heavy growth in dextrose broth at room temperature first noted by Paterson (1939B), is sometimes helpful in recognizing *Listerella* species

The morphologic and biochemic characters of *Listerella* have been studied by Seastone (1935), Webb and Barber (1937) Schultz Terry Brice and Gebhardt (1938), Barber (1939) Biester and Schwarte (1939), Julianelle (1940, 1941B) Graham Hester and Levine (1940B) Cole (1941) and Harvey and Faber (1941B) Probably the most extensive study is that of Harvey and Faber who reported the characteristics of fifty strains of *Listerella* from animal and human sources More recently investigations have been conducted on specific growth requirements of organisms by *Porter and Pelczar (1941) and Hunter (1942)*

The organism grows quite well on plain agar (see Fig 32) small colonies bluish by transmitted light can be distinguished in 24 hours The organism grows still better on blood agar with a clear hemolytic zone which helps to differentiate the colonies *Listerella* strains ferment rhamnose dextrose *levulose lactose maltose sucrose* trehalose dextrin and salicin with acid production Other sugars such as arabinose raffinose inulin dulcitol mannitol sorbitol and inositol were not attacked Galactose was only occasionally attacked Some sugars are fermented slowly

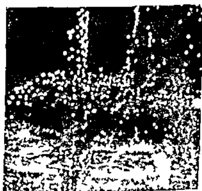


Fig 32—Culture of *Listerella* From Medulla of a Cow Naturally Infected The culture was incubated for 48 hours at 37 C on plain agar *Illinois Agri Exper Sta Bull 499*

Experimentally the natural syndrome has occasionally followed the intranasal instillation of viable cultures at the Illinois Agricultural Experiment Station In support of intranasal infection Pons and Julianelle (1939) reported that an organism which was probably *Listerella* was isolated from the throat of a girl whose blood contained *Listerella* while Gill (1933) reported that repeated drenching of sheep with the culture by way of the nostril resulted in meningitis and encephalitis On the other hand Julianelle (1940) reported that spraying the culture into the noses of rabbits and monkeys failed to produce the disease whereas feeding the culture to mice in place of drinking water caused death in all cases Further investigation is needed to establish the mode of infection

DIFFERENTIAL DIAGNOSIS

The isolation and identification of *Listerella monocytogenes* is regarded as conclusive evidence of the malady Histopathologic changes marked by perivascular infiltration is suggestive of *Listerella* encephalitis Myocardial and hepatic degeneration in chickens and rodents also suggests *Listerella* infection but the isolation of *Listerella monocytogenes* is required in confirming a diagnosis

Serologic tests have proved of no value in detecting infected animals This disease however can generally be detected in ruminants by careful study of the history and symptoms Other diseases which cause nervous symptoms might be confused with listerellosis Therefore bacteriologic examination is required to confirm clinical diagnosis

THE DISEASE IN ANIMALS

The clinical symptoms and pathologic lesions associated with listerellosis vary with the host species In the rabbit guinea pig and gerbille a generalized septicemic infection associated with a circulating monocytosis and necrotic foci of the liver is characteristic In the chicken the disease is characterized by focal but massive necrosis of the myocardium The fox from which *Listerella* was isolated by Cromwell Sweebe and Camp (1939) suffered from a distemper like disease Jones (1940) reported isolation of *Listerella* like organisms from the organs of 14 out of 27 cases of equine periodic ophthalmia but their taxonomic relation to *Listerella* seems inconclusive

Listerellosis in ruminants is usually manifested by an encephalitis

there were relatively few rats and listerellosis did not occur The disease reappeared the next winter when the rats were again numerous On another farm where ovine listerellosis occurred no livestock had been kept for several years previous to the time when the disease appeared but on this farm too the buildings were overrun with rats Olafson (1940) suggested that the rat might be the carrier of the disease The Illinois Agricultural Experiment Station examined 5 live rats and 2 dead ones from a farm where the disease occurred At autopsy no gross lesions were observed in any of the rats The heart blood liver pharynx and colons of all 7 rats and the *lungs of 2* were cultured on plain agar plates but *Listerella* was not recovered However the possible relation of rats to spontaneous outbreaks of the disease merits further study

Observations indicate that in ruminants the disease does not sweep rapidly through the herd Ordinarily less than 10 per cent of the herd may be affected Isolated single cases have also been observed While the morbidity is thus relatively low the mortality in affected animals is very high Few animals that show marked symptoms of the disease recover Young animals are more susceptible than adults and the disease seems to run a more rapid course in them Sheep are apparently more susceptible than cattle since the death losses among sheep are higher and death often follows a shorter period of illness (Tables 20 and 21 show losses of sheep and cattle in Illinois)

Table 21 —LOSSES FROM LISTERELLOSIS IN OUTBREAKS AMONG CATTLE IN ILLINOIS

OUTBREAK No	ANIMALS IN HERD	ANIMALS DEAD		OUTBREAK No	ANIMALS IN HERD	ANIMALS DEAD	
		Number	Per cent			Number	Per cent
1	68	3	4 4	6	40	3	7 5
2	—	1 (abortion)	—	7 (1st herd)	173	[illegible]	2 9
3	15	2	13 3	(2d herd)	110	2	1 8
4	30	2	6 7	8	20	1	5 0
5	—	1	—				

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The avenues of infection in ruminants have not been determined but it is possible that *Listerella* enters the nasal passages This supposition is partially supported by the fact that experimental listerellosis similar in all its aspects to the natural disease *is not ordinarily* produced by intravenous or subcutaneous inoculation or by feeding

are recorded as predominately lymphocytes or monocytes may depend upon the organism and the host The foci of neutrophilic infiltration may or may not have vascular relations Olafson (1940) considers this lesion the most characteristic of the infection since it is said to contain the bacteria the perivascular infiltrations do not

Less constant lesions are focal and perivascular edema or hemorrhage or both and degenerative changes in the nerve cells and tracts Cell inclusions have not been observed This fact and the fact that attempts to reproduce the disease with bacteria free filtrates from infected tissues have failed would indicate that a fil

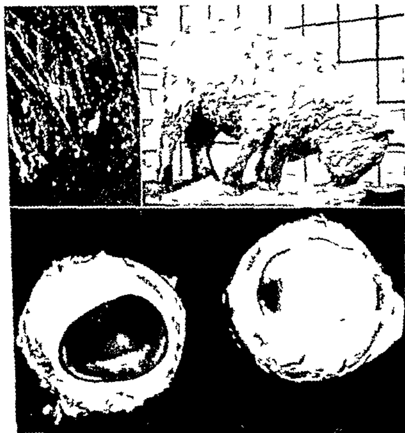


FIG 33—Natural Listerellosis in Sheep The culture of *Listerella* from the sheep medulla (*upper l ft*) was incubated 19 hours at 37 C The large white masses are medulla tissue The eye of the sheep shown below to the right is affected with keratitis the other is normal *Illinois Agri Exper Sta Bull 499*

or encephalomyelitis Meningitis may also be present Bovine abortion unaccompanied by cerebral disturbances has been reported by Graham Hester, and Levine (1939, 1940A) and by Evans and Sawyer (1942) and in sheep by Paterson (1939A 1940D)

The encephalitic syndrome in sheep and cattle is preceded by symptoms of dullness and impaired vision In fact in some outbreaks the first observed symptom has been refusal to come to the feeding racks though not all affected animals exhibit symptoms of inappetence High temperatures may be noted in the first stages of the disease The animal walks into feed bunks or other objects or close to them before observing them In some outbreaks the first observed symptom may be a staggering unsteady gait As the disease progresses the animal begins to circle either to the right or the left and to push or lean against solid objects (see Fig 33) Circling is especially characteristic of the disease in sheep and cattle Torticollis may be observed If the head is placed in normal position it returns to the side as soon as released

A mucous nasal discharge is noted in some animals Quite frequently one ear droops and in some cases the animal drools stringy saliva and shows apparent paralysis of the pharynx (See Fig 34) The animal though able to drink slowly may be unable to eat

Conjunctivitis and opacity of the cornea of the eye have been noted (see Figs 33 and 35) As the disease progresses the affected animal is unable to rise Some animals perform running movements while lying on their sides In sheep this causes the wool to come off and decubital sores to appear on the shoulder and hip The animal becomes progressively weaker accompanied by coma lasting several hours or a few days before death

In experimental listerellosis the nature of the histopathologic changes depends to some extent upon the route of infection Virulence of the organism may also be a factor, as pointed out by Schwarte and Biester (1942) When microscopic lesions are present *they follow a rather constant pattern according to the organ affected* Lesions produced by the natural infection among ruminants are largely limited to the central nervous system *(Figure 36) In the* central nervous system the disease is characterized by perivascular infiltration with cells among which lymphocytes and monocytes predominate focal areas of infiltration or necrosis and infiltration with neutrophiles Some of the foci fulfill all the requisites for true suppuration Whether the cells found in the perivascular infiltrations

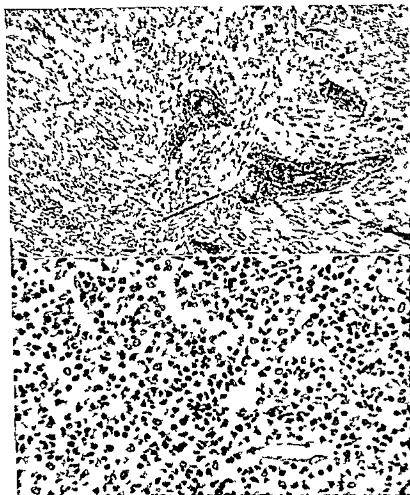


FIG 36—Brain Stem From A Sheep Naturally Infected With Listerellosis Perivascular infiltration with lymphoid and mononuclear cells and necrosis of neurons are shown above magnified 100X Below is shown focal cellular reaction in which neutrophiles predominate (magnified 300X) *Illinois Agri Exper Sta Bull 499*

Liver lesions when present in cases of listerellosis in rodents are noted as discrete foci of necrosis sometimes preceded by visible fatty changes in the cells (Pirie 1927) and later surrounded by hepatic cells showing fatty changes (Webb and Barber 1937) Necrosis is thought to appear in the hepatic cells surrounding Kupffer cells which have ingested numerous organisms according to

trable virus is not a factor in listerellosis That there is some unrecognized factor in natural infection is suggested by the difficulty with which the infection is produced experimentally The distribution of lesions in the brain suggests the possibility of spread by way of the meninges, canal systems and vessel sheaths



Fig 34 —Feeder Calf Affected With Listerellosis Note the drooling and the drooped ear *Illinois Agri Exper Sta Bull 499*

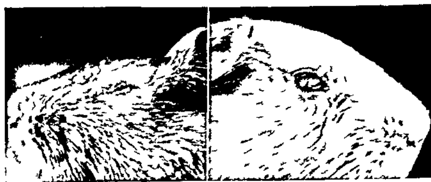


Fig 35 —Guinea Pigs After Suprajunctival Exposure to *Listerella* Both guinea pigs have conjunctivitis the one to the right has keratitis also *Illinois Agrl Exper Sta Bull 499*

Eye lesions consist of conjunctivitis which may be catarrhal or follicular in nature keratitis characterized principally by destruc tion of epithelium and mild infiltration with leucocytes mainly neutrophiles and extension of the capillary system into the substan tia propria of the cornea Other lesions have seldom been observed or have not been well described

THE DISEASE IN MAN

Listerellosis in man has been reported in California Connecticut Iowa Missouri and North Carolina and in the following countries Argentina Australia Denmark France Italy Scotland and Uru guay The mode of transmission is not known

In man the disease always involves the central nervous system In thirteen of the reported cases it was associated with meningitis in four cases with infectious mononucleosis and in two cases with meningo encephalitis

Among the histopathologic changes described in human lister ellosis by Burn (1936) and Wright and Macgregor (1939) the more prominent and constant changes were suppurative leptomen ingitis focal areas of necrosis in the liver focal pneumonia and bronchiolitis and splenic engorgement Also observed in the brain were hemorrhages and perivascular infiltration with neutrophiles lymphocytes and plasma cells

Nyfeldt (1929 1932) and Schmidt and Nyfeldt (1938) reported the isolation of *Listerella* from a number of cases of infectious mono nucleosis of which it was believed to be the cause Pons and Julia nelle (1939) obtained a true *Listerella* from a single case of infec tious mononucleosis but further study by Julianelle (1940 1941A) indicates that the association was probably incidental Subsequently Nettleship (1942) reported that infectious mononucleosis in man is caused by a filtrable virus

PREVENTION AND CONTROL

No universally effective preventive measures are known Isolation of sick animals seems effective in some herds in others the disease may fail to subside until the animals are turned out on pasture Thus it is quite evident that the epizootiology of listerellosis deserves fur ther investigation with special reference to the carrier feature the natural reservoir of infection and the mode or modes of transmission Experimental vaccines and antiserums have been employed experi

Webb and Barber (1937) and Bianchi (1930) The foci of necrosis enlarge and often become infiltrated with neutrophiles or mono nuclear cells or both

Myocardial lesions (Figure 37) consist of necrosis of the heart muscle and cell infiltrations among which mononuclears usually predominate

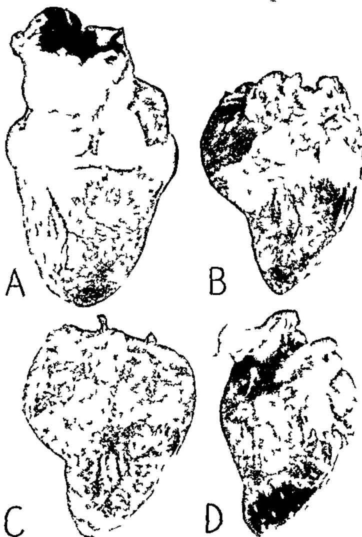


Fig 37 —Massive and Focal Necrosis of the Myocardium Heart A is normal Hearts B and C show massive necrosis and Heart D focal necrosis in chickens that died following intravenous inoculation with *Listerella Illinois Agri Exper Sta Bull 499*

oculation This characteristic of *Listerella* is an aid in identifying the organism

7 Histopathologic studies indicate that the essential character of the lesion in a given tissue is the same in the experimental infection as in the naturally incurred disease In the brain lesions are likely to be more numerous in the white than in the gray matter and are constituted mainly by focal infiltrations of neutrophiles and by perivascular infiltration of lymphoid and mononuclear cells In animals which develop systemic infection foci of necrosis and infiltration with lymphoid and mononuclear cells may be observed in the liver and heart

8 Attempts at immunization of rabbits guinea pigs chickens and sheep against listerellosis by means of killed (and in some cases living) *Listerella* cultures were unsuccessful

9 Attempts at immunization of rabbits guinea pigs sheep and cattle against listerellosis by means of antisera were unsuccessful In some cases the administration of antiserum apparently rendered the animals even more susceptible to experimental infection

10 Little success was obtained with sulfanilamide in the treatment of clinically affected sheep

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mentally in natural outbreaks and experimentally in guinea pigs and rabbits with irregular and unfavorable results

Sulfonamides may be of value in treating cattle and sheep but only if administered very early and in large doses Once encephalitic symptoms develop it is probably too late to institute therapy with much hope of success The problem then becomes one of recognizing new cases and starting treatment as early as possible The most promising approach in detecting new cases is a study of the body temperatures of apparently normal animals in affected herds since the temperature is usually elevated in the initial stages of the disease

ITEMS OF NOTE

1 Listerellosis is a specific bacterial septicemia in rodents and chickens In man it is characterized chiefly by meningitis in ruminants and swine by encephalitis Abortion in cattle and sheep has also been reported as due to *Listerella* and premature birth has been experimentally induced by inoculating pregnant ruminants with viable cultures of *Listerella*

2 In its usual encephalitic form the clinical symptoms make it possible to recognize affected animals easily Listerellosis can be confirmed by bacteriologic examination of the medulla at autopsy

3 Listerellosis occurs most commonly in winter and early spring when animals are closely confined No specific effective preventive measures are known Sanitation and isolation of the affected animals and good pasture in season are apparently helpful in checking the spread of the disease in some outbreaks

4 Sulfonamides administered in large doses have on occasion *given encouraging results but only when administered very early* and in large doses

5 The causative organism *Listerella monocytogenes* is Gram positive and rod shaped It is approximately 0 5 by 1 micron is characterized by a tumbling type of motility and causes beta hemolysis Growth occurs quite well at room temperature as well as at 37° C

6 In experimental listerellosis in cattle sheep rabbits guinea pigs swine and chickens the distribution of lesions varies with the route of *inoculation Conjunctivitis and keratitis* which are occasionally observed in the natural disease in ruminants may be quite readily induced in rabbits and guinea pigs by supraconjunctival in

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CHAPTER VIII

RABIES *

RABIES is an acute infectious disease caused by a neurotropic type of filtrable virus The disease is primarily an affection of the canine race especially dogs but it may affect any of the warm blooded animals Secondarily it is a disease of man transmitted usually by the bite of a rabid dog The term hydrophobia (from the Greek fear of water") may be applied to the disease in man but it is not truly descriptive of the disease in dogs The term rabies (from the Latin "to rave") may designate the disease in any animal but there are times when it is not descriptive as in dumb rabies

HISTORY

Rabies is a disease of great antiquity in fact one of the oldest known diseases of animals Plutarch asserted that according to Athenodorus it was first observed in mankind in the days of the Asculapiadae the descendants of Aesculapius the god of medicine Whitmore relates that in the thirteenth century B C Akteon son of Aristeus died of the disease In the fourth century B C Aristotle stated dogs suffer from madness which puts them in a state of fury and all animals which they bite when in this condition become also attacked with madness Man was considered immune however at that time

Celsus in the first century A D was the first to give a good description of the infection in man using the term hydrophobia He states that the disease is caused by a bite of a rabid animal and the wound must be thoroughly washed in water and burned with a hot iron in order to prevent the development of the disease for after symptoms develop there is no cure and death always follows Park

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believes that Celsus probably obtained his information from earlier writings which have since been lost

Celius Aurelianus in the second century A D, gave a very good account of the disease in man

In the beginning of the attack anxiety with no reason for it irritability and malaise restless movement light sleep and disturbed insomnia stretching and continual gaping and an unremitting desire to vomit an unusual susceptibility to air no matter how quietly the patient may have been resting intoleration and loathing of liquids little desire to drink When the disease is established there is thirst and at the same time dread of water at first at the sight of it later of the very sound or mention of it This fear extends to oily preparations The pulse is small hard and irregular in certain cases there is a light fever There are eructations heaviness of the limbs The diaphragm is displaced upward and the functions of the intestines suppressed Urination becomes frequent and of small amounts There is nervous spasm and trembling The voice is hoarse like the bark of a dog breathing is difficult the body drawn up Generalized convulsions are occasioned by the entry of persons for fear that they may be bringing water The face and eyes are congested the body emaciated Pallor and sweating of the upper parts Frequent erections and seminal emissions The tongue is protruded there is hiccough bilious vomiting frequently black fear to drink the hands being held before the eyes on the approach of the drinking vessel etc (Stimson)

Other writers of that period and in the centuries that followed mentioned rabies without adding to the knowledge of the disease During the middle ages reference to it seemed to have disappeared from medical writings although it is mentioned in other sources In 1271 it is related that in Franconia thirty persons perished from bites inflicted by rabid wolves which invaded the towns attacking people flocks and herds Likewise in Paris in 1604 an epidemic of rabies prevailed

mals for the purpose of diagnosis In 1821 Magendie and Breschet identified human rabies with the disease in animals by infecting a dog with saliva from the human case In 1829 Hertwig showed that the usual method of infection was the saliva of rabid dogs trans mitted by bites All of these observations were corroborated by other investigators

During the period of renewed scientific activity after a lapse of nearly two thousand years it is only natural that false ideas and inaccurate observations should confuse the people For instance Morgagni and Swinger among others believed the bite of a dog not suffering from rabies might initiate the disease Some of the causes ascribed to such spontaneous origin were ungratified sexual instinct in male dogs sudden suppression of lactation in female dogs ex tremes of temperatures especially of heat drinking foul water eat ing putrefied materials or the deprivation of meat from dogs which had been accustomed to a meat diet Contrasted to these notions were those brought forward by Bosquillon in 1902 that hydrophobia was due to fright and that belief in an infectious agent was a chimera

It is difficult to realize the hysteria of the populace in those times in connection with rabies Shooting strangling poisoning or suf focating were not uncommon deaths meted out to victims who were even suspected of exposure to the disease In 1810 a bill was pre sented in Germany to the effect that it is forbidden under pain of death to strangle suffocate bleed to death or in any other way murder individuals suffering from rabies As late as 1819 it was related in France that an unfortunate victim of rabies was smothered to death between two mattresses

In the midst of such confused and hazy notions and opposed by many persons in high stations Pasteur began his work in 1880 on the spread and control of rabies He was able to demonstrate at will the transfer of the virus from animal to animal He showed that dogs protected by virus attenuated by drying were refractory to the dis ease On July 6 1885 after great hesitancy but urged on by the belief that the victim would surely perish otherwise Pasteur ad ministered the first human inoculation of anti rabic vaccine to Joseph Meister a nine year old Alsace boy This was the beginning of a new era in the control of rabies

Diagnosis of rabies in dogs had been carried out by Pasteur as well as by many others through subdural inoculation of brain mate

rial into the rabbit This process required two or three weeks or more making it of small value to any person exposed to the disease Wilson working in the New York City Health Department Laboratory found that this period was ordinarily of shorter duration in guinea pigs such animals often developing the disease in about nine days after inoculation This shorter period of incubation in guinea pigs is by *no means constant More recently the mouse has been proved* to be a valuable test animal After intracerebral inoculation of this species symptoms usually develop within seven to ten days, followed by death on the ninth to twelfth day

In 1903 Negri observed in the brain cells of rabid animals the now well known Negri bodies which are pathognomonic of rabies Negri s findings were soon confirmed by numerous investigators and today the demonstration of Negri bodies in the brain tissue of animals suspected of having rabies is positive evidence of the presence of such disease

SEASONAL PREVALENCE

The fallacy that rabies is a summer disease is based upon the fact that during the months of July and August the dog star Sirius rises with the sun In ancient times this was attributed as the cause of dogs going mad hence dog days However, during this period dogs have much greater freedom than in the inclement weather of winter thus more opportunity for contact with each other In reality there is not a distinct increase of rabies during the summer months Due to the hot weather very often dogs become cross and are suspected of rabies when they are not infected

In 1910 Stimson (1) tabulated figures from different parts of the world to show that there was little variation in seasonal prevalence except that the last quarter of the year showed relatively fewer cases—January to March 25 per cent April to June 27 4 per cent July to September 25 2 per cent and October to December 21 3 per cent of all cases

In figures collected from various sources it would seem that the spring months often show the greatest number of cases with the peak in March (2) The Hygienic Laboratory in a report covering the years 1909 19 for the District of Columbia showed a similar finding Reports from Kansas and New Jersey for the year 1926 likewise indicated a somewhat greater prevalence of the disease during the spring months In the State of Illinois the peak seemed to be

delayed until June and July but August and September were the months of low incidence in all cases There was then a gradual rise through the fall and winter months to the peak in the spring or early summer

There are numerous instances of serious outbreaks of rabies in certain localities during other seasons of the year so as previously indicated there is no marked variation in seasonal prevalence of the malady

GEOGRAPHIC PREVALENCE

Rabies knows no geographic boundaries nor is it subject to terrestrial or climatic influences There are only a few portions of the globe where the disease does not exist and the only reason for its absence in those places is eternal vigilance in keeping it out From the frigid vastnesses of the Arctic region to the sultry atmosphere of the tropics it has been reported From the congested quarters of New York Chicago London and Paris to the sparsely settled wilds of Russia it exacts its toll

Under ordinary conditions the incidence of rabies is directly proportional to the population in a given district In sparsely settled regions the rate is not as great as that of more densely populated areas except in cases where the wild animals become infected In parts of Russia rabies among wolves has existed to a considerable extent likewise in the mountain regions of some of the western states in the United States the disease among coyotes and other wild animals has made its eradication difficult On the other hand rabies exists to a large extent in the thickly settled portions of the world except where the most energetic measures have been taken to prevent its introduction and spread

In the United States there has been a definite increase in rabies during the past few years The increase has been largely in lower animals approximately 10 500 cases being reported to the Bureau of Animal Industry United States Department of Agriculture for the year 1944

In 1926 Rice and Beatty (3) published statistics on the world prevalence of rabies which would tend to show very little difference in twenty years in geographical prevalence As these data are still of interest they are included here Conditions incident to war may be found to have changed these data when the information is available

CANADA

Alberta—No record of any case in ten years

British Columbia—Only one case in any animal known and this was in a dog brought in by a tourist No human deaths

Manitoba—Some rabies in animals No human deaths

New Brunswick—None since 1918 No records previous to that date

Nova Scotia—None in animals or man

Ontario—After several years of freedom from the disease it was introduced from Quebec and quickly spread 41 positive brains were examined in 1926 No human deaths

Prince Edward Island—No data

Quebec—Rabies spreading rapidly from two foci No human deaths

Saskatchewan—No rabies 1926

Alaska—Not common but has been observed particularly in wolves and foxes

Arctic Regions—Nansen mentions the occurrence of rabies in *Farthest North* and it has been reported from Greenland

Mexico—Rabies is very common There are many Pasteur Institutes and thousands of treatments are given annually The number of human deaths is rather large but exact information is not available

SOUTH AMERICA

Ecuador—Not common

Venezuela—Rare in animals and extremely so in human beings

Argentina—Fairly prevalent

Brazil—Has been epidemic at different times especially in the north

From incomplete returns it is reasonable to conclude that the disease is present in moderate amount in the greater portion of the continent of South America

Cuba—Has been epidemic to a serious degree in recent years

El Salvador—Present

EUROPE

Belgium—Has had very little rabies except during the Great War when anti rabic precautions were relaxed During times of

peace elaborate precautions are taken to prevent its introduction These methods have been highly effective

England—By strict muzzling ordinances England was able to rid entirely the country of the disease in 1902 After that time there was none until 1918 when the disease was reintroduced It spread rapidly but has again come under control and there has been none since 1922

France—The homeland of Pasteur has long been seriously plagued with rabies In 1913 it was almost eradicated but flared up again during and after World War I to alarming proportions

Germany—The rabies situation was well in hand before 1914 there being on the average 300 to 400 cases in animals annually In 1915 it rose to 1 018 after which there was an irregular increase to 2 699 in 1924 Since that date the condition has improved and is greatly reduced in 1927 Human deaths were as follows 1924 48 1925 20 1926 22 Persons bitten by rabid dogs for the same years were 2 417 1 159 and 579 respectively

Holland—Because of very rigid control measures there were no cases of rabies in Holland previous to World War I During that crisis there were some in the borders of the country

Ireland—There has been no rabies for twenty years All immigrant dogs are quarantined for six months

Russia—No communication was received from this country but it is well known that the rabies situation is very serious perhaps the worst of any country in the world

Sweden—There has been no rabies since 1886 when there was one case in an imported animal Strict regulations govern the importation of all members of the dog family

Switzerland—Rabies is rare 329 Pasteur treatments were given in the quarter of a century just closed with one human death

Austria—Has been epidemic in recent years

Italy—No very recent data but has been quite common for a long time

Balkan States—Has been an important problem here since World War I and the years immediately preceding

Spain and Portugal—Rabies very important public health problem

Africa

Egypt—Very common among the countless homeless dogs Little effective control of the situation The number of cases treated

trebled from 1914 to 1924 but has decreased since 1 251 treatments were given in 1926 in Cairo alone

Union of South Africa—Fairly common in animals and occasional cases in human beings

Occidental French Africa—Rabies present but not prevalent

Western Africa—Rabies is common

Asia

Palestine—Rabies is very common

Arabia—Common in the settled portions

India—Data from the Pasteur Institute at Calcutta for the Province of Bengal (population 40 000 000) 1924 (seven months) 1,995 patients treated of whom 17 died 1925 5 585 cases treated of whom 33 died Total deaths for Bengal (human) 304 in 1925

Japan—A very serious public health problem

China—Rabies was known in the time of Confucius and has been a serious problem continuously to this day

Siam—Very common

Siberia—Very prevalent

Tibet—Prevalent

Oceanic Islands

Australia—Free of rabies and always has been so

Hawaii—Free of rabies All animals from foreign ports are quarantined for 128 days

Philippines—Rabies is very common among the many dogs Human deaths were 103 in 1925 93 in 1926

Dutch East Indies—Fairly common

THE ETIOLOGIC AGENT

The infectious agent of rabies belongs to the group of ultramicroscopic, filtrable viruses Under suitable conditions it can be passed through V N and W Berkefeld candles and F and B Chamberland filters

The virus is found constantly in the nerve tissue and saliva much less often in the urine lymph and milk and only occasionally in the blood and other body fluids of infected animals It may be present in the saliva five days before the animal shows symptoms

Virus obtained from naturally infected animals is designated as "street virus When the virus has been passed serially through a

large number of rabbits however its virulence is so exalted that it will kill the animals in as short a time as six days and this marked virulence remains constant through subsequent passages Such mod ified virus is known as "fixed virus (virus fixe of Pasteur)

Rabies virus cannot be propagated artificially in lifeless media However Kanazawa (4) in Japan and Webster and Clow (5) in the United States have shown that it can be grown in tissue cultures containing living embryonic mouse brain Plotz and Regan (6) re ported the cultivation of the virus in a medium of Tyrode solution monkey serum chicken plasma and chick embryo cells Dawson (7) has also published successful results in cultivating rabies virus by intracerebral inoculation of day old chicks and then passage to chick embryos

Rabies virus is not very resistant to unfavorable environment Sunlight destroys it rapidly while exposure to air and drying soon renders it inert Boiling immediately destroys it but a temperature of 58 C requires 30 minutes The ordinary disinfectants require more time for its destruction than for bacteria—30 minutes for phenol in 5 per cent solution 15 minutes for bichloride of mercury 1 1 000 3 per cent liquor cresolis and 1 per cent formalin Glycerin serves as an excellent preservative the virus remaining active for weeks or months in it Putrefaction does not ordinarily destroy the virus until after a considerable period of time but putrefied brain tissue is usually difficult material in which to demonstrate Negri bodies

In 1903 the Italian investigator Negri working at Parvia, de scribed certain characteristic bodies in the brain cells of dogs dead of rabies The large ganglion cells of the hippocampus major and the Purkinje cells of the cerebellum were especially apt to show them The bodies were round or oval in shape varying in size from 0 5 of a micron to 22 microns the larger ones showing distinct granules when properly stained Negri considered the bodies not only diagnostic of rabies but the cause of the disease The presence of the bodies in the brain cells of rabid animals was soon confirmed by numerous investigators in Europe and America and thus the well known method of laboratory diagnosis of rabies was estab lished

Schoening (8) in 1925 working in the Bureau of Animal Industry of the United States Department of Agriculture encountered a strain of "street virus which appeared to possess immunogenic

properties which differed from other viruses in that ordinary antirabic vaccines did not protect dogs against it Hampil and Roberts (9) and Habel (10) have also published studies indicating variation in the immunogenic properties of rabies fixed virus Kelser believes that the difference is not due to the existence of immunologically distinct types of rabies virus, but to difference in virulence

RABIES VACCINE

The preparation of all antirabic vaccine up to the present time has been based upon Pasteur s original method—namely the use of nerve tissue from animals which have been infected with the disease

As has already been indicated Pasteur found that the virus of rabies could be stabilized in virulence by passing it successively through a relatively large series of rabbits Thus street virus" which after subdural inoculation was found to require 12 to 25 days to produce rabies in rabbits was brought up to the point where it would regularly cause the disease in 6 or 7 days Its virulence remained fixed at such point and was therefore, designated by Pasteur as virus fixe or fixed virus

Pasteur found that when the spinal cord of a rabbit dead of fixed virus rabies was dried over caustic potash the virulence of the cord, within certain limits was reduced in proportion to the amount of drying Thus a portion of a cord which had been permitted to dry for five days when emulsified and injected subdurally into rabbits required approximately eight days to produce rabies A cord dried nine days required about two weeks to produce the disease whereas a cord dried for 14 days would as a rule cause no symptoms at all Pasteur based his method of antirabic vaccination on this phenomenon

Starting with an emulsion of apparently avirulent cord subcutaneous injections were administered to exposed individuals on consecutive days each day using a cord of a little more virulence In Pasteur s original method the cords used were dried from a maximum of fourteen days to a minimum of three days in the case of "light" treatments When an individual was severely bitten especially about the face and hands an intensive treatment was given This involved the use of cords dried from the maximum of fourteen days to a minimum of only one day The light treatment extended over a period of eighteen days the intensive twenty one

days Table 22 indicates the scheme of antirabic vaccination followed in Pasteur's original method

Table 22 —PASTEUR'S ORIGINAL SCHEDULE OF ANTIRABIC VACCINATION

Light Treatment			Intensive Treatment		
Day of Treatment	Age of dried cord	Amount of injected emulsion	Day of Treatment	Age of dried cord	Amount of injected emulsion
	Days	c c		Days	c c
	14	3		14	3
First	13	3	First	13	3
	12	3		12	3
Second	11	3		11	3
	10	3		10	3
Third	9	3		9	3
	8	3	Second	8	3
Fourth	7	3		7	3
	6	2		6	2
Fifth	6	2	Third	6	2
Sixth	5	2	Fourth	5	2
Seventh	5	2	Fifth	5	2
Eighth	4	2	Sixth	4	2
Ninth	3	1	Seventh	3	1
Tenth	5	2	Eighth	4	2
Eleventh	5	2	Ninth	3	1
Twelfth	4	2	Tenth	5	2
Thirteenth	4	2	Eleventh	5	2
Fourteenth	3	2	Twelfth	4	2
Fifteenth	3	2	Thirteenth	4	2
Sixteenth	5	2	Fourteenth	3	2
Seventeenth	4	2	Fifteenth	3	2
Eighteenth	3	2	Sixteenth	5	2
			Seventeenth	4	2
			Eighteenth	3	2
			Nineteenth	5	2
			Twentieth	4	2
			Twenty first	3	2

The original Pasteur method of antirabic vaccination has been modified in a number of ways The dried cord method was varied by commencing treatments with cords dried less than fourteen days Thus a number of Pasteur laboratories adopted an eight day cord as the maximum of attenuation and still later the Pasteur Institute of Paris went to a five day cord as the maximum of drying The strain of fixed virus first used by the Pasteur Institute in 1888 has been in use ever since Table 23 indicates the dried cord treatment plan which the Pasteur Institute at Paris developed

For a number of years the Hygienic Laboratory of the United States Public Health Service (National Institute of Health) produced and administered Pasteur rabies vaccine to exposed individuals who resided in or came to Washington to receive treatment

The cords used were dried for a maximum of six to a minimum of two days in ordinary cases and one day in severely exposed instances

Table 93—SCHEDULE OF ANTIRABIC VACCINATION AT PASTEUR INSTITUTE PARIS IN 1927

DAY OF TREATMENT	AGE OF CORD	AMOUNT INJECTED
		c c
First day	5	3
Second	5	3
Third	4	3
Fourth	4	3
Fifth	3	3
Sixth	3	3
Seventh	4	3
Eighth	3	3 For slight wounds
Ninth	2	3
Tenth	4	3
Eleventh	3	3
Twelfth	2	3
Thirteenth	3	3
Fourteenth	3	3
Fifteenth	2	3
Sixteenth	4	3
Seventeenth	3	3 For multiple wounds
Eighteenth	2	3
Nineteenth	3	3
Twentieth	3	3 For serious wounds
Twenty first	2	3
Twenty second	3	3
Twenty third	3	3
Twenty fourth	2	3 For wounds on the head
Twenty fifth	2	3

The Hogyes modification is based upon observations made by Ferran in Barcelona in 1888 who used fresh fixed virus diluted 1 100 for treating persons bitten by rabid dogs Boreggi in 1889 was not as successful losing five patients apparently infected by the vaccine It has however been subsequently shown by many workers that fresh fixed virus injected subcutaneously in high dilution is relatively harmless In 1897 Hogyes began its use and since that time many thousands of persons have received this form of antirabic treatment It consists of injections of fresh fixed virus highly diluted followed by gradually increasing amounts of the virus Hogyes maintained that the Pasteur method of drying the cord attained nothing more than a dilution of the virus and that this could be more accurately controlled by dilutions with salt solution Another advantage brought out by Harvey and McKendrick was the smaller amount of nerve tissue in proportion to the amount of virus

Another modification of Pasteur s method is that developed by

Harris The virus cord and brain together are frozen with carbon dioxide snow and finely ground up The material while still frozen is placed in vacuum desiccators over sulphuric acid and dried at a temperature of −15° to −18 C After this the powder is sealed up in tubes in vacuo in the proper amounts for treatment and stored below the freezing point ready for use The powder is emulsified in salt solution when injected The amounts of material gradually in crease as the injections proceed The method is economical in that large amounts of material can be prepared at once and it will re- main potent for six months or longer Ordinary treatments require ten injections while serious cases take fourteen

The Cumming method consists in inactivation of the virus by dialysis in distilled water Emulsified nerve tissue is dialyzed 24 hours in a collodion sac after which time the material left in the sac no longer is capable of producing rabies when injected sub durally into rabbits but still retains its protective value It is ad ministered in amounts of 2 c c over a period of 15 to 25 days

The Semple method is a form of antirabic vaccination which has come into rather extensive use during recent years The brain and cord are emulsified together diluted to 8 per cent and the virus killed with 1 0 per cent carbolic acid which is allowed to act for 24 hours at 37 5 C The mixture is then diluted with an equal quantity of sterile physiological saline solution This constitutes the vaccine Fourteen injections are given for human treatments Some labora tories produce a vaccine with a higher percentage of fixed virus tissue even up to 20 or 25 per cent The dose however is regulated so that a patient receives no more than the equivalent of 2 c c of a 5 per cent emulsion daily At the present time the Semple type vac cine is employed to a greater extent than other forms of rabies vaccine

In 1922 Alivasato published the results of studies which tended to indicate that an etherized rabies vaccine was superior to some of the immunizing agents prepared by older methods According to Aliva satos technic brains from rabbits succumbing to inoculations of rabies fixed virus are stripped of their membranes and immersed in sulphuric ether Some of the brains are allowed to remain in the ether for 72 hours while others are subjected to its action for a period of 84 hours Following the exposure to the ether the brains are cut up into small pieces in sterile dishes and placed under a bell jar or in a desiccator in order that the ether may evaporate One

part of the brain tissue is then emulsified with twenty parts of physiological saline solution This constitutes the finished vaccine The first two doses consist of 1 5 gm of the suspension of brain tissue which was exposed to the action of ether for 84 hours This is followed by *additional injections of vaccine prepared from the brain* tissue which was subjected to the ether treatment for only 72 hours

Alivasatos vaccine was employed rather extensively in India a few years ago However, it is now but seldom used

Kelser developed a chloroform treated rabies vaccine which was found to possess some advantages over phenol killed agents This vaccine, for human use consists of a 25 per cent suspension of brain and cord tissue to which has been added 1 per cent chloroform for the inactivation of the fixed virus Daily doses of 0 5 c c each over a period of fourteen days constitute the treatment

Webster (11) several years ago reported the results of preliminary experimental studies with a tissue culture vaccine in rabies immunization While this method is still in an experimental stage it is possible that it may be improved to the point where it will supplant some of the older methods

During the past 25 years considerable work has been done with vaccines for the immunization of dogs against rabies Most of this work has involved the use of single injections of vaccine Eichhorn started the practice by introducing in the United States the vaccine prepared by the method of Umeno and Doi of Japan This is a phenol treated vaccine and it or a modification of same has been used on a relatively large scale in many sections of the United States

Kelsers chloroform treated rabies vaccine for the immunization of dogs consists of a 33⅓ per cent suspension of brain and cord tissue from rabbits dead of fixed virus rabies the virus being inactivated through the addition of 1 per cent chloroform This type of vaccine has likewise been used to a considerable extent in the United States

RABIES IN ANIMALS

All warm blooded animals including man are *highly susceptible* to rabies Birds and fowls are somewhat less susceptible while cold blooded animals such as frogs turtles etc are refractory

Rabies is primarily a disease of the canine race—dogs wolves coyotes etc The lessened prevalence in certain animals may be the result of the relatively infrequent contact with other species which

might harbor infection or possibly because of natural protection like a thick fur which would mechanically remove the virus that would otherwise gain access to the wound

The relative incidence of rabies occurring in different animals has been given by Stimson in tables collected from different sources The dog leads with 80 per cent to 90 per cent of all cases followed by the other domestic animals and finally the wild animals At the Hygienic Laboratory of the United States Public Health Service (National Institute of Health) over a ten year period 588 animal heads were diagnosed positive for rabies of which 514 were dogs 34 cats 32 cattle 5 hogs and one each sheep horse and man At the laboratory of Illinois State Department of Public Health over a four year period there were 416 positive animal heads of which 393 were dogs 18 cats 2 cows 2 skunks and 1 wolf

The incubation period of rabies varies depending upon several factors—the kind of animal afflicted the kind of animal responsible for the injury whether the wound is near the head or not and the virulence and amount of virus entering the wound Reichel has given the incubation period of rabies in the domestic animals as follows

Dogs fourteen to sixty days
Cats fourteen to sixty days
Cows fourteen to eighty days
Horses twenty one to ninety days
Hogs twenty one to sixty days
Sheep twenty one to sixty days
Goats twenty one to sixty days
Birds fourteen to sixty days
Rabbits nine to ninety days
Guinea pigs eight to sixty days

It is very rare for rabies to develop after the one hundredth day from the bite although a few such instances have been reported

Natural immunity is enjoyed by only certain of the lower vertebrates as the reptiles Under ordinary circumstances death is the inevitable result when an animal becomes infected

A very few apparently authentic cases are on record of recovery of dogs from an actual attack of the disease They are exceedingly rare

The dog is the natural reservoir of rabies from which the disease spreads to other animals The dog manifests symptoms in two differ

ent forms which are designated as *furious* rabies and *dumb* or *paralytic* rabies The form the disease assumes apparently depends on the virulence of the virus, the resistance of the animal and the sequence of localization of the virus in vital brain centers For example fixed virus which has been exalted in virulence, producing the disease in a short period of time gives rise to the paralytic form of rabies even in dogs horses etc, when injected subdurally

Furious rabies in the dog is responsible for the spread of most cases of the disease After a stage of development lasting one or two days in which the animal may be unusually depressed or unusually affectionate he has an irresistible tendency to roam Often many miles will be covered in the next two or three days during which time he will bite anything that happens to come in his way Rarely however does he willfully attack man or other animals that *are not in his immediate path He will attempt to eat indigestible* articles as sticks stones and rags His appearance may not be abnormal enough to attract attention though usually he looks like a sick animal The foaming at the mouth which sometimes appears, results from an accumulation of saliva due to difficulty in swallowing coupled with constant champing" of the jaws When the animal returns home from his roaming he seeks a secluded spot and develops paralysis and soon dies

Infrequently a dog presents no signs of frenzy or irritability and the first symptoms noticed are those of paralysis—so called dumb rabies *The animal hides away develops paralysis in the lower jaw* followed quickly by the rest of the body and dies in one to three days

Cats develop rabies fairly frequently and with danger to human beings especially children The animal hides itself in a dark corner or under the furniture from which it sallies forth in vicious attacks on persons who come near It will jump up and severely scratch the face of a child The voice is lost the animal mewing hoarsely The appetite is later lost with emaciation paralysis and death in a few days

Cattle are often affected with rabies as a result of bites from rabid dogs or other animals and are capable of doing considerable damage due to their size and strength Both the furious and the dumb types may occur the former being the more common After a preliminary stage marked by a change in the disposition of the

animal together with a loss of appetite lessened flow of milk and restlessness the furious type develops The animal paws the earth attacks everything in sight with its horns and bellows loudly with a peculiar change of voice About the fourth day it becomes more quiet and develops paralysis dying in a day or two more

It is said that skunks may propagate the disease widely among their own kind Skunks have been known to attack persons also It is not uncommon to receive skunks in the laboratory for examination for rabies According to Stimson animals other than dogs and skunks do not transmit the disease as a rule more than one remove from the dog The relative inability inopportunity or lack of tendency to bite when rabid is given as the cause for this

In 1931 Hurst and Pawan (12) reported a rather extensive outbreak *of paralytic rabies in man and cattle in Trinidad and found* that the same was transmitted by the vampire bat Subsequently Torres and de Queirez Lima (13) discovered that hematophagous bats (*Desmodus rotundus murinus*) when naturally or artificially infected commonly resist the disease themselves but become reservoirs of the virus and infect animals they bite when obtaining a blood meal An excellent article on the vampire bat as a vector of rabies has been published recently by Gilyard (14)

Rats and other rodents are very susceptible but it is unlikely that the disease is very often propagated among them Their rather limited contact with man renders them of small danger

Birds such as fowls and pigeons are susceptible to inoculation but show a relative immunity many of the older ones recovering The high body temperature of birds 108 F may be the cause of apparent immunity

Cold blooded animals are not very susceptible Several workers among them von Lote and Marie succeeded in infecting frogs but the incubation period was extremely long Negative results were obtained by other investigators The tortoise is refractory to rabies

THE DISEASE IN MAN

Rabies in man follows a course not unlike that in animals Both the dumb and furious types are met with The incubation period may vary from fourteen to ninety days according to the location and extent of the wounds If the head and face are badly lacerated symptoms may appear in as short a time as ten days if the wound

is on an extremity and slight symptoms may be delayed for weeks or months. Several cases of an incubation period over a year have been reported.

Many persons bitten by rabid animals escape the disease even without treatment. The virus may be wiped off from the teeth by the clothing or there may be an individual immunity among certain persons. At the Pasteur Institute in Paris it was found that only 16 per cent of persons bitten by rabid animals but receiving no treatment contracted the disease. Bites on the exposed surfaces, such as the face and hands, are much more dangerous than bites on other parts of the body. It is common experience that a bite on the hand is almost as dangerous, with an incubation period as short, as when the wound is located on the head.

The incidence of rabies in man is fairly well indicated by the number of deaths reported, since the disease is invariably fatal. For the twenty-four year period 1920-1943 in the United States Registration Area, human deaths varied from 36 to 105 per annum.

Table 24.—HUMAN DEATHS FROM RABIES FOR PERIOD 1920-42 INCLUSIVE
(From U. S. Public Health Service)

STATE		STATE	
Alabama	60	Nebraska	7
Arizona	11	Nevada	0
Arkansas	35	New Hampshire	2
California	64	New Jersey	42
Colorado	5	New Mexico	3
Connecticut	3	New York	39
Delaware	2	North Carolina	63
Dist. of Col.	0	North Dakota	[illegible]
Florida	30	Ohio	85
Georgia	79	Oklahoma	65
Idaho	5	Oregon	3
Illinois	88	Pennsylvania	82
Indiana	47	Rhode Island	6
Iowa	17	South Carolina	52
Kansas	28	South Dakota	7
Kentucky	54	Tennessee	113
Louisiana	38	Texas	99
Maine	2	Utah	2
Maryland	9	Vermont	1
Massachusetts	32	Virginia	23
Michigan	36	Washington	8
Minnesota	1	West Virginia	37
Mississippi	52	Wisconsin	8
Missouri	72	Wyoming	0
Montana	2		

During this same period, investigations and surveys were made by various individuals. Sellers for the period 1917-21 found 168 human deaths in 28 states, or an average of 33 per year. *Eichhorn's* figures for 34 states in 1921-23 were 35, 34, and 37 per year. The

studies of Hull as well as those of Rice and Beatty indicate that human deaths were increasing in the United States In 1927 Beatty reported 92 deaths

From the standpoint of mortality rabies is a disease of childhood according to figures gathered from the United States Registration Area by the Metropolitan Life Insurance Company Six deaths out of every ten from this disease occur among children under fifteen more deaths occur between five and ten years than for any other age group Boys are more often victims than girls seven out of ten deaths of children under fifteen years are males Not only are children more often attacked by rabid dogs than adults but the incubation period in children is shorter allowing less time for protective inoculation

Table 25—HUMAN DEATHS FROM RABIES IN THE UNITED STATES
(From U S Public Health Service)

1920	54	1928	105	1936	73
1921	69	1929	85	1937	59
1922	50	1930	60	1938	66
1923	65	1931	55	1939	39
1924	80	1932	52	1940	41
1925	93	1933	65	1941	39
1926	97	1934	80	1942	36
1927	93	1935	77	1943	47

The control of rabies in man rests entirely upon prevention After symptoms of the disease appear there is no known cure Antiserums have been tried by several investigators Babes in 1890 used serum alone while Marie used an anti sheep serum mixed with vaccine Chicken serum has also been tried but results have been unsatisfactory

PREVENTION OF RABIES

The prevention of rabies in man may be accomplished by either of two methods—the treatment of persons bitten by rabid animals or the elimination of rabies in dogs

THE TREATMENT OF PERSONS BITTEN BY RABID DOGS

The efficacy of antirabic vaccine has been demonstrated many times At the Pasteur Institute in Paris from 1886 to 1905 29 101 patients were treated with 122 deaths a mortality of 0 41 per cent from 1906 to 1924 16 741 patients were treated with 29 deaths—a mortality of 0 17 per cent from 1925 to 1927 there were 2 055 patients treated with no deaths At the Pasteur Institute in Chicago

from 1890 to 1910 there were treated 4,463 patients with a mortality of 0 13 per cent From 1910 to 1927 there were 2 467 patients with no deaths

The usual cause for death after treatment is delay in beginning the vaccine injections Deaths occurring within fifteen days after treatment cannot necessarily be charged against the treatment Other possible causes for failure are several There may be a particularly massive dose of infection introduced into the wound or the strain of virus may be of unusual virulence Extensive wounds about the face and hands are frequently followed by an incubation period of such short duration that treatment fails The response of the individual person to vaccine treatment must be likewise taken into account The potency of the particular vaccine employed is another important factor While in rabies there are no statistics in other diseases occasional persons are found who do not become immunized with a single series of injections Immunity as all other biologic phenomena is relative and not absolute

The period of protection gained by a course of antirabic treatments is not very long Experimental work with dogs would indicate that a course of treatments affords protection for eighteen months in that animal In man the time appears to be somewhat shorter Park describes a case in which the immunity did not last fourteen months The man employed in a hospital for dogs received an eighteen course treatment after a slight wound from a rabid dog Thinking himself immune he became very careless one day putting an abraded hand into the mouth of a rabid dog Six weeks later he developed hydrophobia—fourteen months after his course of treatments Sivori Rebaudi has used the power of the blood serum to neutralize rabies virus as an indication of the immunity of an individual Maggiulli found that in man the highest potency of the serum was reached thirty five days after completion of treatment Earlier than eighteen days after beginning of treatment or later than one year the serum of vaccinated persons acts just the same as that of unvaccinated persons

The unfortunate accompaniment of antirabic treatment is an occasional case of paralysis with sometimes fatal results Various factors have been ascribed as the cause of this condition Roux Laveran and other early workers considered the symptoms due to an abortive type of *street virus rabies modified from the usual* symptoms by the course of injections Fabricius and Nedrigailoff

and Ostrjanin as well as others found that paralysis sometimes occurred when the wounds were slight or even when the biting animal was proved not to be rabid Other explanations advanced are that it is a fixed virus infection that outside infection is introduced with the virus that hysteria is responsible for the symptoms or that a rabies toxin may cause the paralysis Anaphylaxis due to injection of foreign protein was suggested by Harvey and McKendrick who called attention to the fact that the Hogyes vaccine prepared by dilution of the nerve substances caused the least number of cases of paralysis This view is given some support by other workers who have found that at times injections of nerve substances from presumably normal animals may cause paralysis

The belief that post vaccinal paralysis is due to rabies fixed virus contained in the vaccine is receiving more support today than previously Kelser (15) has studied this complication in dogs and has recovered fixed virus from animals given single injections of rabies vaccine for prophylactic purposes He found that where phenol treated rabies vaccine contained occasional relatively coarse particles of brain tissue live virus could often be demonstrated in same Live fixed virus injected subcutaneously with large amounts of foreign nerve tissue will result in rabies much more often than when unaltered fixed virus is administered in a highly diluted form with relatively little nerve tissue

Kelser believes that most cases of post vaccinal rabies are due to fixed virus He considers those cases which have a localized paralysis as a peripheral type of fixed virus rabies in which one or more nerve trunks are involved but in which the central nervous system escapes invasion because of partial immunity conferred by the vaccine A large percentage of such cases recover Where the central nervous system is involved, a generalized type of disease results and the mortality is high

With the variety of types of rabies vaccine available for the treatment of individuals exposed to rabies the physician is often at a loss to know which type to select This is a unique situation because ordinarily one form of a particular biological agent—presumably the best—dominates its field until a better form is developed and proved The older type is then usually replaced with the improved product In the case of rabies vaccines however a multiplicity of same is and has been available for years

Many students of filtrable viruses hold the opinion that it is

impossible to immunize a person or lower animal against a virus disease with vaccines or other agents containing dead virus If this be so then any rabies vaccine in which the virus is biologically dead would be worthless A more likely view held by others is that killed virus will immunize provided sufficiently large quantities are used For this reason there has been a tendency during the past few years to increase the amount of virus containing brain and cord tissue entering into the preparation of the so called "killed virus" rabies vaccine As previously pointed out the injection of large amounts of a concentrated suspension of foreign nerve tissue is conducive to the development of fixed virus rabies if viable virus of such type is present in the vaccine It is therefore, essential in the manufacture of these vaccines of high tissue content that every precaution be taken to insure inactivation of all of the virus present

Simon (16) in 1913 collected figures in 92 950 cases which had received antirabic treatment The original Pasteur method was used in 32 676 cases with 6 paralyses—1 in 5 446 the modified Pasteur method was used 8 657 times with 16 paralyses—1 in 541 the Hogyes method was used 51 417 times with only 3 paralyses—1 in 17 139 Mejio in 1917 published figures on 19 800 cases treated at the Pasteur Institute Buenos Aires with 24 paralyses and 4 deaths At the New York City Health Department among 6 738 cases treated there were seven cases of paralyses and two deaths

The following well known rules for the care of suspected animals and recommendation for antirabic treatment are given

When a dog acts suspiciously or when he bites a person he should not be killed On the contrary the dog should be securely confined in a safe place and provided with his regular food supply during an observation period of two weeks In all cases where it is possible to do so the dog should be placed under the observation of a veterinarian If it remains well and healthy throughout the two weeks *he may be released* and any person whom *he may have* bitten need have no fear of coming down with rabies because of the bite If on the other hand the dog should manifest the symptoms of rabies during the observation period he should be allowed a day or so to progress to the advanced stages of the disease and then be destroyed He should not be shot through the head but should be disposed of in such a manner that the head may be detached without mutilation packed in ice in a double container and delivered or expressed to the laboratory

The Pasteur treatment should be commenced immediately upon making a diagnosis of rabies Where the animal has been under the observation of a veterinarian and is diagnosed clinically as rabies treatment should be started without waiting for the laboratory report If from a clinical standpoint there is doubt as to whether or not the disease which the dog under observation has developed is actually rabies treatment may be delayed pending the laboratory examination except in cases of individuals who have received severe wounds about the face and head region or hands In such latter instances the time element is important so treatment had best be commenced immediately and if the subsequent laboratory examination and circumstances warrant it can be discontinued

HOW TO TREAT DOG BITES

First—Call a physician The doctor will properly cleanse cauter ize and dress the wound so that the possibility of infection from any disease including rabies will be less likely to occur than other wise

Second—The dog should be captured alive if possible and placed under veterinary observation as indicated above As Negri bodies which are diagnostic of rabies are usually not demonstrable in the brain cells of animals destroyed in the early stage of the disease it is important that the animal be kept alive until the malady has progressed well towards the final stages After the animal is de stroyed the head should be detached without mutilation and for warded to a laboratory where examinations for rabies can be made

Third—If the dog is known to be rabid the Pasteur antirabic treatment should be started at once If rabies develops in the dog during the period when he is under observation or if the diagnostic examination of the head shows the presence of rabies the Pasteur treatment should be started at once upon learning either of these facts In case rabies cannot be positively ruled out even though it cannot be definitely established the Pasteur treatment is indi cated

WHO SHOULD TAKE PREVENTIVE TREATMENT

The fact that a person is or has been bitten by a dog does not mean that he should take the Pasteur treatment The Pasteur treat ment is necessary and is recommended for only those persons who have been exposed to the bite of a rabid animal It has already been

indicated that Pasteur treatment occasionally gives rise in itself to a so called treatment paralysis Fortunately the incidence of this complication is low and where the administration of rabies vaccine is indicated there should be no hesitancy whatever in proceeding with the treatment On the other hand a patient should not be subjected to the slight risk of post vaccinal paralysis by giving him rabies vaccine to be on the safe side when a careful study would clearly show that the treatment was unnecessary

Persons who should take the Pasteur antirabic treatment may be classified as follows

(a) Those who have been bitten scratched or otherwise wounded by an animal KNOWN to be rabid

(b) Those who have fresh open wounds in the skin which have been exposed to the saliva of an animal KNOWN to be rabid

(c) Those who have been bitten or otherwise wounded by a sick animal that has exhibited the symptoms of rabies even though a definite diagnosis of rabies has not been and cannot be made

(d) Those who have been bitten by apparently healthy animals which were subsequently destroyed or which escaped or could not be definitely identified so that they could not be observed in the manner described

Cautery of wounds was a common practice before the discovery of antirabic vaccine A red hot iron was the means of accomplishing the procedure Fuming nitric acid has been found to be the only other efficient agent Tincture of iodine and phenol come next but these agents are less efficacious

While drastic cauterization on an extensive scale is not warranted under present day procedures of treating individuals exposed to rabies infection there are many instances where the type and location of the wound and the time elapsing since its infliction make a rational type of cauterization a worthwhile procedure

THE ELIMINATION OF RABIES IN DOGS

The elimination of rabies in the dog—and it is possible—would prove much more far reaching and efficacious in preventing hydrophobia in man than treatment after being bitten by a dog

The methods aiming at elimination of the disease among dogs are two—restraint and vaccination In either case it is necessary to destroy ownerless dogs This is an expensive and unpleasant task often involving the city authorities in controversies with irate but neglect

ful citizens who have lost their pets In many cities where other preventive measures have been taken with great care much of the effort is nullified because the important factor of the stray animal is neglected



Fig 38 —Proper type of dog muzzle allowing dog to open its mouth for respiration while still preventing it from biting

The restraint of a dog can be accomplished by locking up the animal leashing it when on the street or effectively muzzling it so that it cannot bite other animals The confinement of dogs to the premises of the owner is a temporary measure for regions badly infected It should last for at least three months however so as to cover the incubation period of any animals that might have been exposed as well as to give the authorities opportunity to eliminate stray dogs Leashing when on the street is an excellent measure provided the leashed dog is in charge of a capable individual Muzzling must be well supervised to insure not only an efficient muzzle but a

humane one The metal muzzle of the basket type properly fitted and changed from time to time with the animal s growth is reasonably satisfactory It must be pointed out that muzzling is frequently improperly done and poorly enforced and under such circumstances is of very limited value in rabies control

The efficacy of the control of rabies through restraint of the dog has been demonstrated in many communities In England it has twice been used to free that island from infection

Vaccination of dogs against rabies with one subcutaneous injection dates from the work of Umeno and Doi in Japan in 1921 They used a glycerinated fixed rabies virus attenuated with carbolic acid with very satisfactory results Hata (17) in 1924 published the results of the first 104 629 dogs so treated in Japan Only 41 of the inoculated animals developed rabies most of which had been exposed before vaccination was undertaken In the control group of less than one third the vaccinated group 1 699 dogs developed the disease

Experimental work by investigators in the United States has confirmed the findings of the Japanese workers Eichhorn and Lyon (18) immunized six dogs with single injections of 5 c c of vaccine Three weeks later these dogs were inoculated intra ocularly with a suspension of brain tissue from three different dogs known to have died from street rabies At the same time three control dogs unprotected by vaccine were similarly infected with street virus The six vaccinated dogs did not develop rabies while the three controls died of the disease in fifteen to seventeen days The work of Reichel and Schneider and of Schlingman was equally conclusive Schnurer in Austria and Schern in Uruguay have also had good results

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On the other hand failures in dogs with the single injection of antirabic vaccine have been noted from time to time In a survey made in 1927, a few cases were reported (2) In Ohio seven dogs developed the disease after vaccination five of which showed symptoms within two days and the other two after three to six

months Arizona one dog after six months Tennessee three dogs after two to three months New Jersey one dog after nine months Virginia two dogs after four to eight months Washington State one cat after one year New York State two dogs after three to six weeks two dogs after four to six months and one dog after a year In Georgia where in one year about 7 000 dogs were vaccinated some cases of failure had been reported but no histories had been obtained

Webster (21 22) Leach and Johnson (23 24) and Johnson (25 26) have published important treatises dealing with the potency and protective value of rabies vaccines

During recent years considerable attention has been paid to the development of a satisfactory potency test for rabies vaccine In 1939 (27) Webster reported results of a potency test in which the mouse was used as the test animal A modification of this test was later reported by Wyckoff and Beck (28) A still further modification was developed by Habel (29) and this test is now commonly employed for the potency testing of rabies vaccines The technic of the Habel test follows

Thirty Swiss mice one month of age 11 to 13 grams in weight all one sex and preferably females are given intraperitoneally 0 25 c c doses of the vaccine diluted so as to contain 0 5 per cent of brain tissue The doses are given every second day for 6 doses Eighteen similar mice are selected and set aside for controls Fourteen days subsequent to the administration of the first dose of vaccine all the vaccinated mice and the 18 controls are challenged with a test dose of fixed virus

In preparation for the challenge not less than 3 mice should be given 0 03 c c of a 10 per cent emulsion of the fixed virus about one week after the first dose of vaccine is administered to the vaccinated mice By such timing the mice inoculated for production of the test virus will develop the disease just at the time the first test virus is required The mice producing the test virus should be sacrificed on the first day of definite symptoms and the brains removed and kept at 0 C until used On the fourteenth day of the test the virus mouse brains are emulsified with sufficient 10 per cent horse serum in distilled water to make a 10 per cent suspension by weight The emulsion is then centrifugalized for 10 minutes at 1000 r p m The supernatant material is then removed and carried through serial ten fold dilutions of from 10 to 10^{7}

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puted by the number of times the dilution giving the end point in vaccinated mice is more concentrated than that in the controls

An attempt was made to compare the effect of vaccination of dogs on the yearly demand for human antirabic treatment The annual report of the Georgia State Board of Health for 1925 states In the first six counties there appears to be a possible decrease in 1925 in rabies as indicated by the decreased demand for treatment In the last four counties listed rabies remained stationary or increased in 1925 Hence no definite conclusion can be drawn

Compulsory antirabic treatment of dogs has been gaining in favor in many places In Japan it became effective in 1923 In Uruguay such a bill was introduced in 1926 In the United States a considerable number of cities municipalities and counties have made rabies vaccination compulsory Congress has recently (1945) passed a law authorizing the Commissioners of the District of Columbia to make rabies vaccination compulsory whenever such action is deemed necessary in the control of the disease The State of Washington required all dogs shipped into the State to be vaccinated with the exception of performing dogs In New Mexico the State Director of Public Health could order all dogs within any area specified by him to be effectively muzzled or confined or else be impounded or killed unless protected by inoculation with a vaccine of a recognized potency In a large number of other communities antirabic vaccination of dogs had been recommended by health authorities and veterinarians and in many instances it had been made optional to other methods of control as in New Mexico Eichhorn estimated that between 1923 and 1926 half a million dogs had been vaccinated in the United States (30) and by 1928 at least two million dogs (31)

In Illinois histories of 454 rabid dogs were studied in 1928 of which 18 had previously been vaccinated The intervals between vaccination and the first symptoms of the disease follow

2 dogs	1 day interval	1 dog	5 weeks interval
1 dog	4 days interval	2 dogs	6 weeks interval
2 dogs	2 weeks interval	1 dog	2 months interval
2 dogs	3 weeks interval	1 dog	[illegible] months interval
1 dog	4 weeks interval	1 dog	4 months interval
2 dogs	1 month interval	1 dog	6 months interval
1 dog		time not given	

To determine the m l d of the challenge virus the 18 control mice are divided into 3 groups of 6 each one group being given intra cerebral injections of 0 03 c c of the 10 dilution of virus the second group the same dosage of the 10^{6} dilution and the third group the 10^{7} dilution At the same time groups of 6 each of the



Fig 39—Improper type of dog muzzle which only serves to irritate the dog and in no way prevents it from biting

vaccinated mice should be given intracerebrally 0 03 c c doses of the 10^{1} 10 10^{3} 10^{4} and 10^{5} dilutions All of these mice should be observed for 21 days and note made of those dying after showing symptoms of fixed virus rabies The m l d is the highest dilution of the challenge virus causing death from rabies in at least 3 of the 6 control mice receiving the particular dilution The "end point" of the immunity in the vaccinated mice is indicated by the lowest dilution of the challenge virus survived by at least 3 of the 6 mice in the group The number of m l d protected against can be readily com

among other dogs for the 50 stray dogs were known to have bitten 108 other dogs (and probably more) while the 65 home dogs bit only 62 others (and probably but few others for many of them were under the observation of a veterinarian) The home dog is more of a meance to persons however for it bites nearly twice as many people as does a stray dog

THE PROBLEM OF MILK AND MEAT

Rabies virus has been found in the milk of infected animals by Nocard Perroncito and Bardach It probably is present in the milk several days before the animal shows symptoms as it is in the saliva Mohler inoculated the milk of a rabid bitch into guinea pigs producing typical symptoms The puppies of the bitch removed from her at sign of the first symptom remained well It is generally conceded that there is no danger from the ingestion of infected milk unless there be abrasions on the lips or along the alimentary tract through which the virus may enter the circulation Mohler cites the case of a woman in the early stages of rabies who transmitted the disease to her nursing baby apparently through the milk but the possibility of abrasions of the gums through teething must be con sidered Other instances are on record where nursing animals have become infected apparently through the milk but the possibility of abraded gums from teething or scratches and bites of the mother cannot be ruled out *Milk from cattle suspected of rabies should not* knowingly be used for human consumption or fed to animals Cows in herds that have been attacked by rabid dogs but where infection is doubtful should be carefully watched for possible symptoms the milk being boiled or pasteurized meanwhile

Persons with cuts on their hands should not milk such cattle as the incubation period draws to a close

Meat from rabid animals as well as brain material has been fed to dogs with no ill results Wyrsykowski showed that the gastric juice quickly destroys the virus He digested brain material with gastric juice and injected twenty one rabbits none of which devel oped rabies seventeen check rabbits injected with undigested ma terial all developed the disease

The use of meat from cattle infected with rabies would be un wise and probably would not take place if the symptoms were well developed It seems to be the custom in some localities when rabies appears in a herd of cattle to rush those animals not already show

It is apparent that the animals developing the disease within a few days after vaccination were in the incubation stage when vaccinated and one injection afforded insufficient protection Those which developed the disease within several weeks after vaccination may likewise have been in the incubative stages or it is barely possible that in some of them the vaccine may have been responsible Whether the animals which developed the disease three to six months later were in the incubation stage when vaccinated is impossible to state The inference is that these constitute cases where the vaccine failed but it may not be so The vaccination may have had some effect upon lengthening the incubation period

At the present time there is some disagreement among various authorities as to just how much reliance can be placed upon the vaccination of dogs in the control of rabies That properly prepared vaccines do increase an animal s resistance to artificial infection with rabies street virus has been amply established by a number of investigators While the administration of single doses of vaccine has been the common practice two or three doses with an interval of a week between doses is a preferable procedure Many cases of natural infection have undoubtedly been prevented by the vaccination of susceptible dogs Vaccination of dogs is thus a justifiable procedure

On the other hand from the evidence accumulated it cannot be said that rabies may be effectively controlled and eliminated solely through the use of vaccines at present available Vaccination while definitely of value should only be considered an adjunct to regulatory measures aiming at the restraint and control of dogs for the prevention of rabies It is possible that investigations with rabies virus artificially propagated in tissue cultures may lead to the development of a rabies vaccine of such increased potency that the universal vaccination of dogs will reduce the incidence of rabies as much as smallpox vaccination has reduced variola in the United States

The role of the stray dog in the spread of rabies is indicated in a study made in Illinois During the summer of 1927 information was collected upon 115 dogs which were positive on laboratory examination at various laboratories in the state Of the 50 stray dogs only 5 had been under the observation of a veterinarian while 35 of the 65 whose owners were known had been so observed It would appear that the stray dog was a serious menace in spreading rabies

methods of control including vaccination can be used to supplement but not to replace these measures

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ing symptoms to the slaughter house to be converted into meat Since the saliva is infective several days before symptoms develop it is probable other portions of the body are infective Butchers and others handling such meat would be placed in danger of infection if abrasions were present on the hands Proper cooking promptly destroys the virus

In general, it can be stated that transmission of rabies through the ingestion of milk meat or other food contaminated with rabies virus is exceedingly rare

ITEMS OF NOTE

1 Rabies is a disease to which all warm blooded animals without exception are susceptible
2 The dog is the important factor in the spread of rabies to other animals and to men
3 Elimination of rabies in dogs serves to eradicate the infection in that vicinity
4 The virus of rabies is an ultramicroscopic filtrable virus
5 After symptoms of rabies appear there is no cure
6 Not more than one person in six bitten by rabid animals develops the disease even though no antirabic treatment is taken
7 Bites on the exposed surfaces as the face and hands are most dangerous
8 Rabies is an abrasion infection requiring a broken skin for entrance of the virus
9 Ingestion of the virus is not dangerous unless lesions are present in the mouth or throat The gastric juice of the stomach quickly destroys the virus
10 Milk from cows suspected of having been exposed to rabies should as a matter of course be thoroughly pasteurized or boiled However infection by this means is exceedingly rare
11 Rabies is an all the year round disease occurring during every month of the year
12 Antirabic vaccine is highly effective in the vast percentage of cases in preventing the disease in man when administered promptly It should not be administered to persons who do not need it
13 The elimination of rabies in a community requires the restraining leashing or muzzling of all dogs accompanied by a strenuous campaign to destroy all stray and ownerless dogs Other

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outbreaks of severe pneumonia which occurred in Paris in 1892 and caused a somewhat similar consternation among the population as the pandemic of 1929 30 The mortality was 33 per cent in a group of 49 patients occupying three different households At first Du jardin Beaumetz concluded that the outbreak was of human origin and not a parrot disease transmissible to man However Peters and later Dubief (January 1893) in a new epidemic concluded that the disease was a specific infectious illness conditioned by contact with an infected parrot The hypothesis of psittacosis as a specific infec tion received strong support from the studies of Nocard (1892) He cultivated from the bone marrow of the dried wings of parrots which had died on the voyage from Buenos Aires some 4 months before a Gram negative motile bacillus pathogenic not only for parrots but fowls mice and guinea pigs both by inoculation and feeding These findings were in part supported by the work of Sicard (1897) who isolated the Nocard bacillus from the blood of a parrot suspected as the source of the infection of 5 patients and the claims of Gilbert and Fournier (1896) in finding a rod resembling the microorganism in the heart blood of a fatal case of psittacosis However Nicolle (1898) and subsequent investigators have failed by repeated cultures from blood urine and feces and by agglutina tion test to furnish any proof whatsoever that psittacosis of parrots and man is a specific disease caused by the Nocard s bacillus (Bacillus or Salmonella psittacosis) Simultaneously with the out break of psittacosis in Paris an epidemic of 8 cases was reported in Duhringsdorf near Landsberg A W in Germany For the first time the disease was associated with a shipment of parrakeets held in a box in a post office building Between 1894 and 1897 limited out breaks of psittacosis occurred in Italy (Florence Prato Udine and Genoa) and were traced to recent importations of Amazon parrots from Buenos Aires The epidemics were stopped after a series of orders prohibiting importations had been issued The first note worthy epidemics of psittacosis in Germany occurred in Cologne in 1898 and in Krefeld in 1899 Amazon parrots and parrakeets were held responsible Leichtenstern in discussing these outbreaks calls attention to the human case to case infections The significance of the famous Zulpich epidemic in the spring of 1909 has not been ap preciated until recently Two apparently healthy parrakeets infected every person—a total of 26—who entered or passed the room where these birds were held Bachem Selter and Finkler isolated strepto

CHAPTER IX

ORNITHOSIS (PSITTACOSIS)

ORNITHOSIS is a virus disease of birds to which man is susceptible Psittacosis is the disease found in the psittacine birds it is widely distributed among wild parrots parrakeets parrotlets cockatoos and related species In recent years it has been found in many bird breeding establishments and pet shops as an acute chronic inapparent and latent infection of parrakeets canaries and finches With increasing frequency single or multiple household or occupational infections among human beings exposed to such sources have been recognized and proven bacteriologically The word psittacosis from ψιττακός (Psittacus) = parrot and suggested by Morange (1895) is primarily used to designate a peculiar contagious disease of man which may follow either fleeting or prolonged exposure in a room store or aviary where visibly diseased or apparently healthy birds are held in captivity

Ornithosis of the domestic hen and the pigeon is becoming increasingly important in the epidemiology of the disease

HISTORY

The scientific report by Ritter in 1879 on a pneumotyphus epidemic among the members of a household who had recently received a shipment of sick exotic birds from Germany for the first time associated a disease of parrots with a new malady of man Sickness and mortality among imported bird consignments had been previously observed and made the subject of etiologic investigations by Eberth Wolf and others In fact it is now known that von Jurgensen already in 1876 had seen and reported on cases similar to those described by Ritter In rapid succession similar house epidemics were observed by Ost (1882) and by Wagner (1882 and 1886) The malady became generally known through the localized

outbreaks of severe pneumonia which occurred in Paris in 1892 and caused a somewhat similar consternation among the population as the pandemic of 1929 30 The mortality was 33 per cent in a group of 49 patients occupying three different households At first Du jardin Beaumetz concluded that the outbreak was of human origin and not a parrot disease transmissible to man However Peters and later Dubief (January 1893) in a new epidemic concluded that the disease was a specific infectious illness conditioned by contact with an infected parrot The hypothesis of psittacosis as a specific infec tion received strong support from the studies of Nocard (1892) He cultivated from the bone marrow of the dried wings of parrots which had died on the voyage from Buenos Aires some 4 months before a Gram negative motile bacillus pathogenic not only for parrots but fowls mice and guinea pigs both by inoculation and feeding These findings were in part supported by the work of Sicard (1897) who isolated the Nocard bacillus from the blood of a parrot suspected as the source of the infection of 5 patients and the claims of Gilbert and Fournier (1896) in finding a rod resembling the microorganism in the heart blood of a fatal case of psittacosis However Nicolle (1898) and subsequent investigators have failed by repeated cultures from blood urine and feces and by agglutina tion test to furnish any proof whatsoever that psittacosis of parrots and man is a specific disease caused by the Nocard s bacillus (Bacillus or Salmonella psittacosis) Simultaneously with the out break of psittacosis in Paris an epidemic of 8 cases was reported in Duhringsdorf near Landsberg A W in Germany For the first time the disease was *associated with a shipment of parrakeets held in a* box in a post office building Between 1894 and 1897 limited out breaks of psittacosis occurred in Italy (Florence Prato Udine and Genoa) and were traced to recent importations of Amazon parrots from Buenos Aires The epidemics were stopped after a series of orders prohibiting importations had been issued The first note worthy epidemics of psittacosis in Germany occurred in Cologne in 1898 *and in Krefeld in 1899 Amazon parrots and parrakeets were* held responsible Leichtenstern in discussing these outbreaks calls attention to the human case to case infections The significance of the famous Zulpich epidemic in the spring of 1909 has not been ap preciated until recently Two apparently healthy parrakeets infected every person—a total of 26—who entered or passed the room where these birds were held Bachem Selter and Finkler isolated strepto

cocci both from the human secretions and the cadavers of the killed parrakeets The Nocard s bacillus was not found

Between 1914 and 1928 single and group infections have been reported from England and the United States The epidemic of 1917 reported by McClintock in Wilkes Barre Pennsylvania originated in the basement of a large department store where many sick parrots *were stored, has since had its counterparts in outbreaks observed by* Badger in New York (1930) and in Pittsburgh (1934)

From a rare and obscure disease psittacosis was suddenly raised into a malady of worldwide interest when in July 1929 Barros informed a number of prominent physicians and later the Medical Society of Cordobas Argentina concerning the appearance of over 100 cases of a serious and peculiar pneumonia among the inhabitants of Cordobas Alta Gracia and Tucuman He diagnosed the disease as psittacosis since the epidemiologic investigations showed that a large consignment of psittacine birds had been imported into Argentina from Brazil that there had been a great mortality among the birds and that from this shipment the patients had purchased the parrots which had fallen ill and in a number of instances had died Local attention was directed to the strange disease in October when in Buenos Aires a theatrical troupe of 12 persons, all of whom fell ill and 2 succumbed following the use on the stage of a parrot which died shortly before the human cases developed The population was now warned and the trade in parrots stopped entirely in the Argentine However, *the passengers of steamers calling at the* Argentinian ports ignorant of the existence of an epidemic disease of parrots transmissible to man bought many of the infected birds from unscrupulous dealers Thus the malady was conveyed to many countries It reached the United States in November 1929 while England reported cases in July and then in December During the early months of 1930 the newspapers gave accounts of outbreaks in at least 12 countries (Austria Italy Switzerland France Denmark Algeria Holland Egypt Czechoslovakia Germany Sweden and United States of America) In many of the reports it was stated that shipments of sick parrots had arrived in those countries Later a perusal of the records of 1930 left no doubt that the South American parrots were not the only sources of infection In England in the United States and Switzerland psittacosis developed following the exposure to love birds and canaries The importance of the parrakeets was only appreciated when K F Meyer and B Eddie in co

operation with the California State Department of Public Health recognized in 1931 and 1932 the wide distribution of latent psitta cosis in the local breeding establishments and aviaries of California (13) Fortner and Pfaffenberg (7) and Haagen and Kruckeberg (9) in extensive studies have fully confirmed the American findings for Germany while Gerlach (8) discovered endemic psittacosis in the bird stores and aviaries of locally bred and raised parrakeets canaries and finches in Austria The parrakeets raised in France were also infected (Aujaleu and Jude 1)

The pandemic of 1929 30 with approximately 750 to 800 cases and the subsequent endemic distribution of parrakeet psittacosis involving the United States and Germany with another 500 cases offered a splendid opportunity to many investigators for a thorough study of the disease from a clinical etiologic and epidemiologic point of view The reports from every country have converged in the same direction and it is now firmly established that psittacosis is an infection with a filtrable corpuscular microscopically demon strable and cultivatable "virus The hypothesis of a *Salmonella* in fection has been entirely abandoned

In 1942 Meyer and his associates called attention to the disease in pigeons with reports of several human infections (20)

PREVALENCE AND DISTRIBUTION

The prevalence of psittacosis is worldwide wherever the parrots and parrakeets are found The records for the period 1876 1928 in dicate that it was recognized in rather rare instances in the United States (4 cases) Brazil France Germany Great Britain and Italy During the pandemic of 1929 1930 it was reported from 22 coun tries—United States Canada Honolulu Argentina Brazil Algeria Australia Austria Czechoslovakia Denmark Egypt France Ger many Great Britain Italy Japan Mexico Netherlands Poland Spain Sweden and Switzerland During the period since that pan demic the number of cases has greatly diminished In the United States a small number have occurred each year (table 26)

Since the diagnosis of a single case is quite difficult and mild and atypical cases frequently accompany severe infections in house hold epidemics it is quite correct to suspect that the actual number of cases of psittacosis is not known The persistence of the disease in Germany and during 1932 to 1934 a high incidence in the United States and California was due to the distribution and sale of locally

bred and diseased parrakeets Despite a tremendous reservoir of psittacosis among the jungle birds very few human infections have been recognized in Australia and Argentina

Ornithosis in pigeons has been reported to an increasing extent from widely scattered parts of the United States

Table 26 —CASES AND DEATHS FROM PSITTACOSIS—UNITED STATES 1929-1942
(U S Public Health Service)

	CASES	DEATHS
1929 1930	170	33
1931	22	8
1932	74	12
1933	15	3
1934	22	9
1935	8	1
1936 (no reports)	—	0
1937	4	1
1938	4	3
1939	9	2
1940	8	3
1941	12	1
1942	32	4
	380	80

THE ETIOLOGIC AGENT

Independently first by Bedson and Western (2) in England Levinthal (12) in Germany Armstrong and McCoy in the United States and Sacquepee in France the virus character of the psittacosis disease agent was established in 1930 Of particular importance has been the discovery by Krumwiede McGrath and Oldenbusch (11) that the virus is readily transmitted to white mice It is now fully recognized that the elementary bodies measuring from 0 22 to 0 36 μ (see Lazarus) and generally described as the Levinthal Cole Lillie bodies or *Microbacterium multiform psittacosis* independently discovered by the three investigators in the exudates blood and organs of diseased birds mammals and man represent the virus They are readily demonstrated in the infective material by the Macchiavello (aqueous basic fuchsin pH 7 4 heated and differentiated with citric acid) or the Castaneda stain The Giemsa and Heidenhain iron haematoxylin stain are sometimes useful Bedson (2) and Bland and Canti (3) have followed in detail in the spleen of mice and tissue cultures the morphologic changes incident to the intracellular growth of these bodies This bacterial parasite which is slightly larger than the Paschen bodies of variola or vaccinia re

veal a 48 hour cycle with five phases in which the early stages as large forms or virus colonies ultimately divide into elementary bodies destroying the host cells In all psittacosis infections whether birds rodents or man the essential injury is the invasion and destruction of the reticulo endothelial system Virus bodies should be searched for in these cells (see figure 40)



FIG 40 —Levinthal Cole Lillie (L C L) bodies of psittacosis in the peritoneal exudate of infected mouse ×3600

On account of its size the filtrability of the psittacosis virus is rather limited Only the more porous types of filter candles or colloidal pads allow the virus to pass Organ suspensions or sputum specimens which are infectious to mice in high dilutions frequently yield non infectious filtrates when passed through Seitz pads or Berkefeld V filters Through fractional sedimentation in angle centrifuges the L C L (Levinthal Cole Lillie) bodies may be secured in a high state of purity The elementary bodies grow freely in the ectodermal cells of the chorion allantoic membrane of the chick for several hundred passages without losing their infectiousness (Bland Burnet and Rountree Lazarus Meyer and Eddie and Fortner and Pfaffenberg) On lifeless media no growth is obtainable However in fluid tissue cultures consisting of Tyrode solution and chick embryo cells (Maitland method) excellent growth has been secured through 40 passages (Yanamura Meyer and Eddie Levinthal

Haagen and Crodel) The infectiousness persists undiminished 0 5 c c of a dilution 10^{-9} is fatal to a mouse in 14 days The elementary bodies are specifically agglutinated by antisera produced on guinea pigs or other animals They act as excellent antigens in the complement fixation test (Bedson Meyer and Eddie) The psittacosis virus contains two antigens one resistant to boiling and the other rapidly destroyed at this temperature (Bedson)

The virus is not very resistant to glycerin but quite so to desiccation Dried by the lyophile method it remains active for over 6 months When exposed to formaldehyde (0 2 per cent) at room temperature the virus remains infectious for periods up to 10 days however it is quite heat labile (15 minutes at 70°C)

Experimentally the virus has been transmitted to a variety of psittacine birds (parrots shell parrakeets) ricebirds sparrows and canaries It should be borne in mind that these birds may carry latent infections (psittacosis and salmonellosis) and that in the infected state they are dangerous sources for laboratory infections The mouse as a universal and relatively safe experimental animal has displaced the birds The gross anatomic lesions in form of an enlarged spleen liver necrosis, a ballooned duodenum peritoneal exudate and occasional patches of pneumonia with cells of the reticulo endothelial system filled with L C L (Levinthal Cole Lillie) bodies are very characteristic (Meyer and Eddie and Levinthal) The rodents may be infected by any route even by feeding and contact exposure Mice inoculated with small doses of the virus survive the infection and may carry the virus for over 200 days or develop a sterile immunity Gophers (*Thomomys bottae*) are readily infected by the subcutaneous route (Hoge) The intratracheal injection of guinea pigs (Fortner Meyer and Eddie) squirrels (Meyer and Eddie) and monkeys (Rivers and Berry) leads to extensive and highly characteristic pneumonic lesions with an abundance of virus Macacus monkeys infected with virus by the subcutaneous route may prove resistant to intratracheal re infection (Rivers and Schwentker) Virus passage through mice stabilizes the infectiousness and maintains the virulence through hundreds of transfers

Ornithosis virus of pigeon origin is closely related and is not to be distinguished from the virus of parrot origin except by its virulence Virus of pigeon origin is of less virulence for man than virus of parrot origin

GENERAL EPIDEMIOLOGY

As a rule the epidemiologic facts in household outbreaks are stereotype in nature suddenly a patient with an atypical pneumonia is observed in a family in which recently a parrot or a pair of parra keets *rarely canaries or finches have been introduced as cage pets* Quite often in rapid succession additional cases are seen among the relatives and even guests or visitors The responsible pet birds may or may not be visibly sick Usually 2 to 3 weeks elapse between the acquisition of the birds and the onset of the first case A seasonal prevalence during the winter months (January April) is probably due to the frequency with which human beings receiving birds as *gifts are brought in contact with them through prolonged exposure* in the closed rooms of a winter household (Meyer Fortner and Haagen) The majority of psittacosis infections have occurred in people of middle age (Elkeles—66 per cent for age group 30 to 50 Sturdee and Scott—60 per cent over the age of 40) The disposition to clinical psittacosis is very low in children under 10 years of age (English data four children under 10 California one German *none*) *Intimate exposure to the same parrakeets which infected the* parents or older relatives failed to induce the disease in children A significant difference in the susceptibility of the sexes has only been noted in the outbreaks due to shell parrakeets (England pandemic 57 males to 60 females California 29 males to 53 females) The greater frequency in women is in part due to the fact that they are either engaged in the breeding of birds or as lovers of pets come more closely in contact with the virus The mortality rate is higher in the groups between 40 and 60 years of age The case fatality rates from 25 to 40 per cent in the outbreaks preceding and during the pandemic (36 per cent for 49 cases in Paris 24 per cent for 167 cases in the United States 20 9 percent for 215 cases in Germany 21 36 per cent for 117 cases in England) have slightly declined during the past few years With the recognition of mild or missed infection the percentages have remained around 18 per cent

Occupational psittacosis is now fully recognized Through the ob servations of Widowitz Roch and Wohlers Prausnitz and Stepp Weber Gerlach Haagen and particularly Meyer and Eddie the oc currence of this disease as an *occupational liability among persons* engaged in the breeding raising transportation and sale of parrots and parrakeets is well known The California statistics with 30 (in

82) proven infections in owners of aviaries leave little doubt that the occupational hazard is quite high Psittacosis among dealers was seen during the Paris epidemic by Barros in Argentina by Brauer in Hamburg and by A Bruce Steele in California The personnel of pet and department stores has suffered greatly from psittacosis (Badger, Hegler and others) Seamen bringing home parrots to sell and baggage car employees shipping parrakeets contracted parrot fever Physicians veterinarians, health department officials and inspectors experienced severe attacks of psittacosis (Leichtenstern Hamel Buchanan Glage Hegler Elliot and Hatfield Haagen and Kruckeberg) During the experimental investigations of avian psittacosis in 1929 and 1930 at least 38 laboratory infections were contracted Despite the institution of precautionary measures an additional 8 cases with 2 deaths occurred in Germany and the United States in the next several years

Human case to case infections are by no means infrequent (Meyer) Professional nurses or persons who care for psittacosis patients are prominently represented Of particular interest is the fact that contrary to the views of many epidemiologists non fatal cases of human psittacosis may infect their nurses The amount of virus in the sputum and the training of the nursing personnel control the secondary infection there is no evidence that the infective agent loses its invasiveness by human passage In fact, Haagen and Kruckeberg report a chain transmission in the third generation (a patient infected his nurse who transmitted the disease to a woman patient of the hospital ward)

The pathways of transmission from bird to man are twofold (a) by the aerogenic route—the inhalation of dust contaminated with infective particles derived from desiccated fecal droppings urine feathers cadavers etc, and droplets from the nasal secretions and (b) rarely by direct contact through bite wounds The high infectivity of the psittacosis virus which resembles that of smallpox or measles is reflected in the histories in which short exposure occurred in a pet shop where diseased birds were kept Contrary to general belief among the laity actual contact or possession of diseased psittacine birds is not necessary since air currents may disseminate the virus particles

Pigeons have been responsible for the disease in man on a number of occasions Meyer Eddie and Yanamura (1942) reported 10 such cases in New York Massachusetts Minnesota and California Other

cases have been reported by Alicandri (21) in New York Levinson Gibbs and Beardwood (19) in Philadelphia Favour (22) in Boston Turgasen (23) in Wisconsin and Shaughnessy in Chicago The virus which is found in pigeons is less virulent for man than is the virus found in the psittacine birds The droppings of pigeons probably contain the virus with human infections occurring by inhalation

The domestic fowl and duck are infected when exposed but they apparently have played a small part in the epidemiology of the dis ease

IMMUNITY

The nature of the lack of disposition or of the acquired immunity is not clearly understood Recovery from an attack of psittacosis or injection of living virus in monkeys (Rivers and Schwentker) may be followed by the appearance of neutralizing antibodies in varying amounts and a persistence of complement fixing antisubstances Per sons constantly exposed to the virus may have a high neutraliza tion index of their blood The resistance to re infection in mice is frequently an infection immunity" associated with the latency of the virus in the viscera Active immunization of mice with formalin treated or photodynamically inactivated antigens protect mice against ten million fold lethal doses of virus However the immunity is not complete the test inoculation may set up inap parent infections lasting for seven months (Bedson) Rivers and Schwentker recommend the active immunization of laboratory work ers with six progressively increasing doses of a 10 per cent mouse spleen psittacosis virus administered intramuscularly at weekly in tervals In view of the inherent tendency of the psittacosis virus to latency this method requires further study

LABORATORY DIAGNOSIS

The blood obtained during illness may contain the virus it should be inoculated either defibrinated or as serum intraperitoneally into mice Bedson and Meyer and Eddie found the blood virulent up to the 4th and 10th day Gerlach even on the 15th and 16th At any stage of the disease the sputum is the most likely material to yield positive findings on inoculation of unfiltered centrifuged or filtered sputum extracts into mice or ricebirds The virus is not always pres ent and repeated examinations are indicated It has been found on the 32nd even the 75th day (Gerlach) after the onset of the disease

At post mortem the infective agent has repeatedly been demonstrated in portions of the lung spleen and liver in the order mentioned

The complement fixation test with heated antigens prepared from spleens of infected mice or cultures and descending serum dilutions has proven of great value in the early diagnosis of the disease provided the patient gives a negative Wassermann reaction Extreme precautions should be exercised since any material containing the psittacosis virus must be regarded as highly pathogenic and dangerous Experimental inoculations should not be attempted except in especially equipped laboratories

THE SPONTANEOUS DISEASE IN TROPICAL BIRDS

The recognition that a variety of tropical birds and in particular, shell parrakeets (*Melopsittacus undulatus*) may act as sources of infection is one of the important contributions resulting from the researches in psittacosis since 1931 Equally far reaching is the discovery that visibly healthy" birds may harbor the virus and as shedders disseminate the infective virus The incidence of these inapparent latent infections in aviaries and breeding establishments may vary from 10 to 90 per cent Although the importation embargoes against South American parrots which were instituted by practically every country following the pandemic of 1929 30 throttled the exotic bird trade but disclosed the existence of endemic psittacosis in the domestic breeding establishments of California Germany Austria France and England With the aid of newer laboratory methods the disease of the birds has been carefully studied (Meyer and Eddie Fortner and Pfaffenberg Haagen and Kruckeberg Garlach Levinthal) It is quite generally admitted that the clinical manifestations of parrots or parrakeets infected with psittacosis are by no means characteristic Sick birds may be recognized by their behavior and appearance sleepiness motionless sitting on the perches ruffled feathers semi closed or closed eyes fits of shivering loss of weight with atrophic breast muscles and labored breathing may be noted Diarrhea with greenish stools or soiled tail feathers with grayish mortar like concretions are occasionally observed The mortality among parrots may be very high while among parrakeets held in a fairly sanitary environment only 5 to 10 per cent actually succumb to psittacosis Young birds are more susceptible than the older ones Through contact experiments the in

cubation time has been found to be from 5 to 20 days and not infrequently much longer (100 days) Relapses are quite common in carefully observed cage birds and the disease may last for weeks In order to prove the psittacosis nature of the parrot or parrakeet disease autopsy and laboratory examinations are important The gross anatomic changes aside from emaciation and in the acute cases septic hemorrhages are not very extensive and are confined

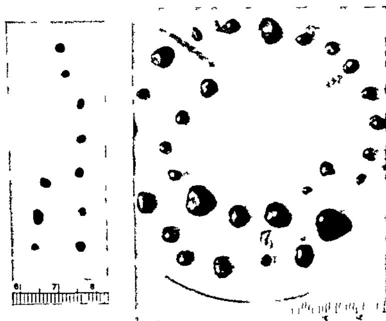


FIG 41—Spleens of parrakeets showing normal spleen (left) and spleens from parrakeets infected with psittacosis (right) 2 5 mm to 10 0 mm in diameter

to the abdominal cavity The liver may be enlarged saffron colored and studded with fresh or partially healed necroses and infarcts catarrhal inflammation of air sacs and degenerative changes in the kidneys

An enlargement of the spleen variable as to size in the different stages of the disease is rarely absent Direct smears from these organs when adequately stained reveal the elementary L C L bodies while organ suspensions infect mice The routine diagnosis of latent psittacosis in parrakeets segregates the non infected from the infected birds by the size of the spleen (see figure 41) Spleens with a

diameter of over 3 to 4 mm yield on inoculation a high percentage of virus infections The histopathologic alterations have been studied by Lillie Thus the parrot disease of psittacine birds is primarily a disease of the liver and spleen with no lesions in the lung and occasional latency up to 812 days in parrakeets

The veterinary differential diagnosis must take into consideration the Salmonella infections which are by no means uncommon in South American tropical birds Psittacosis and salmonellosis may exist in a carrier stage in the same parrotlet The so called Pacheco virus disease of parrots studied by Rivers and Schwentker must be considered in the examination of diseased parrots

Spontaneous psittacosis infections responsible for human disease have been proven in the following species of the order *Psittaciformes* Blue fronted Amazon (*Amazona aestiva*), various Cuban Mexican and Panama species (*Amazona barbadensis* Gmelin) macaw (*Ara ararauna*) short tailed parrot (*Graydidasculus brachyurus* Temminck and Kuhl) shell parrakeets or budgerigars (*Melopsittacus undulatus*) sulphur crested cockatoos (*Kakatoe galerita*), galah (*Kakatoe roseicapilla*) and Murrum bidgee smoker parrots (*Barnardius sp*) Enzootic acute and latent psittacosis among wild parrots and parrotlets has been demonstrated by mouse tests in the following Australian species Shell parrakeets, lorikeets (*Trichoglossus chlorolepidotus* and *moluccanus* 58 per cent) grass parrot (*Psephotus haematonotus* 41 per cent) cockateels (*Leptolophus hollandicus* 60 per cent) roseleas (*Platycercus sp*) African species Mask (*Agapornis*) and ring necked parrakeet (*Palaeornis torquatus*) and South American species Spectacled parrotlet (*Psittacula conspicillata*) Spengel parrotlet (*Psittacula spengeli*) and brown throated conures (*Eupsittula pertinax aeruginosus*) Experimentally a great many other species have been successfully infected with the psittacosis agent for example senegal parrots (*Poeocephalus senegalus*) conures (*Conurus solstitialis Eupsittula canicularis E cacurum*) orange bellied grass parrakeet (*Neophema chrysogastea*) Quaker parrakeet (*Myiopsitta monachus*) African love birds or masks or peach faces (*Agapornis roseicollis personata*) etc Combining all these findings the uniform disposition of the psittacine birds to psittacosis is fully established and further evidence strongly supports the belief that the infection is widely distributed among wild parrots and parrakeets perhaps as a population regulator The high incidence of prolonged latent infections in certain species par

ticularly those desired as cage birds is important Crowding lack of sunlight and of cleanliness and malnutrition so prevalent in transit and in bird stores diminish the resistance of the birds to the infective agent lying dormant in the tissues The active psittacosis which follows not only exposes other birds but becomes the main source of human infections

THE SPONTANEOUS DISEASE IN FINCHES

Epidemiologic observations by Roubakine Sturdee and Scott have definitely incriminated the canary bird (*Serinus canaria*) while Meyer and Eddie and more recently Gerlach proved conclusively the role of this finch as a potent source for human psittacosis infections In fact various other finches thrushes and sparrows [goldfinch (*Carduelis carduelis*) bullfinch (*Pyrrhula pyrrhula*) nonpareil (*Cyanospiza ciris*) Lady gould finch (*Poephila mirabilis*) blackbird (*Turdus merula*) crossbill (*Loxia curvirostra*) titmouse (*Parus major*) siskin (*Spinus spinus*) yellow crowned sparrow (*Zonotrichia*) Bengalese (*Uroloncha acutocauda*) pekin robin (*Liothrix luteus*)] exposed in bird shops or accidentally fed on contaminated seeds from infected stores (Gerlach) may contract the disease and spread it to other birds and even man (in Holland fire finch *Lagonosticta senegala L*) Particularly susceptible are ricebirds (*Padda oryzivora*) they are used as sentinels in aviaries to detect the presence of the psittacosis virus among apparently healthy parrakeets (Meyer and Eddie) Chickens exposed in breeding pens with diseased budgerigars have contracted psittacosis (Meyer and Eddie)

THE SPONTANEOUS DISEASE IN PIGEONS

Ornithosis of pigeons is probably widespread in the United States Meyer Eddie and Yanamura studied flocks from many different areas of the country and found that 30 per cent to 75 per cent gave positive complement fixation reactions The virus was isolated from many of the birds tested

The virus possesses a highly adapted latent parasitism for pigeons similar to psittacosis virus for parrots Parrakeets and ricebirds are fatally infected by feeding or inhalation of the pigeon strain of virus Pigeons (and an occasional dove) are clinically not affected by feeding or intramuscular injection but continue to carry the virus for many weeks in their organs

Infection seems to be acquired when the pigeons are young in the nest or soon after Adverse conditions, such as crowding in insanitary cages or improper feeding causes a flare up of the disease

The droppings are suspected but have not been proved to be the cause of transfer of infection

THE DISEASE IN MAN

The clinical manifestations listed in the numerous histories of severe cases are remarkably uniform (Adams Sturdee and Scott Gorham Calder and Vedder Polayes, Maclachlan Permar and Rogers Rabinowitz and others) The incubation time although difficult to establish in many instances varies from 7 to 15 days after initial contact Since an incubationary latency cannot be excluded it is not surprising to observe occasionally an incubation time of from 30 to 39 days The onset of the disease may be abrupt or begins gradually and insidiously with indefinite influenza like symptoms like malaise anorexia headache backache photophobia and chills Restlessness insomnia delirium typhoidal state non productive cough constipation, occasionally diarrhea with abdominal distension and tenderness are as a rule present during the height of the infection Epistaxis occurs in about 25 per cent of the cases Rose spots may appear on the pale icteric skin The temperature rises rapidly and assumes the character of a continuum which may begin to fall by lysis during the second or third week One of the characteristic features of the disease is the relative slowness of the pulse compared with the temperature In the fatal cases the pulse becomes rapid and feeble The spleen is rarely palpable Phlebitis with thrombosis are frequent complications The lungs are involved in every case except the mild and ambulatory cases Physical signs may develop slowly and have a peculiar migratory character roentgen ray examinations indicate that the parenchymatous consolidation begins early in the course of the disease As a rule the cough when present is not productive despite extensive respiratory involvement, the sputum is scanty (sputumless pneumonia) mucoid and very rarely rusty or blood tinged Due to secondary infections the ensuing bronchitis produces a copious frankly purulent sputum A remarkable feature of the disease is the frequent absence of rapid or deep breathing even when the physical signs in the lungs indicate extensive involvement In the second week encephalitic manifestations in form

of lethargy stupor etc may make their appearance In fact the apathy and toxemia are entirely out of proportion to the clinical signs of exhaustion and organic involvement White blood counts reveal a leucopenia or a slight leucocytosis Convalescence is very slow and tedious relapses are by no means rare Mild and ambulatory cases may last for one day to one week and are only recognized in the course of epidemiologic investigations No effort should be spared to make an etiologic diagnosis by examination of nasal washings or sputum specimens in the mouse test or the complement fixation test of the serum (see below) Symptomatic treatment and good nursing are essential Human not necessarily convalescent sera with a high neutralization index possess curative properties

The morbid anatomy of 52 cases were admirably summarized by Lillie in 1933 Anatomically the focal or lobular pulmonary consolidation involves the alveolar epithelial cells which desquamate and become embedded in a serous exudate poor in polymorphonuclear leucocytes Interstitial infiltration is usually lacking and the bronchioles may remain clear In the hematopoietic system congestion and phagocytic activity prevail while in the liver focal necrosis of the parenchyma and vacuolation of the Kupffer s cells are found

Gerlach by sputum examinations of 2 persons exposed to clinical cases of psittacosis has indicated the probable existence of inapparent silent human infections According to Haagen the virus may persist in the spleen for at least 2 weeks after recovery from acute psittacosis

Zichis and Shaughnessy have reported two fatal cases of pneumonia due to virus of pigeon origin (24)

PROTECTIVE AND PREVENTIVE MEASURES

Psittacosis of psittacine origin could be readily controlled provided the public would appreciate the possible danger inherent to contact with birds psittacine varieties or finches particularly of unknown origin However the love for pets so deeply rooted in human nature cannot be changed Some degree of protection has been obtained by means of restrictive measures such as embargo of exotic birds quarantine isolation etc During 1930 practically every country prohibited the importation of parrots including any bird of the group known as Psittaciformes" However gradually exceptions have been adopted In the light of present day knowledge on

the inapparent infections, it is doubtful what effect the detention of imported birds for a period of two weeks may have on the entire psittacosis situation of a country However since the commercial aviaries engaged in the breeding and raising of shell parrakeets are the principal spreaders of diseased birds and the creators of epizootics among canaries and finches in pet shops etc every effort should be made to create a bird industry free from psittacosis Efforts along these lines have been made in California Germany Austria and elsewhere Connecticut New York and Oregon maintain a permanent quarantine against psittacine birds

In California anyone engaged in selling, trading or bartering shell parrakeets must obtain a certificate of registration (Senate Bill No 516 Chapter 607 1933) According to regulations, the aviaries are subject to two laboratory tests before they may be certified and the birds released for sale The first test consists of mature birds 6 months of age or over and represents 10 per cent of the entire stock The second test consists of immature birds The spleen of the parrakeets removed at autopsy are tested by mouse inoculations

Laboratory tests have shown that these procedures associated with improved sanitation have progressively reduced the incidence of latent infections as follows

1932 January to 1934 June	89 aviaries 55 (61 per cent) harbored infected birds
1934 July to 1934 December	193 aviaries 48 (24 8 per cent) harbored infected birds
1935	79 aviaries 3 (3 8 per cent) harbored infected birds
1936	*28 aviaries no infected birds*
1937	1 aviary infected

If the laboratory tests are negative for psittacosis then the aviary is released The birds of the aviaries must carry a leg band with a code number assigned to them by the State Department of Health For interstate shipment the United States Public Health Service requires a certificate issued by the State These control measures have not interfered with the economic phase of the problem Annually between 30 000 and 36 000 parrakeets are shipped interstate

The German law of March 7 1934 provided for the detection of infected aviaries through laboratory tests destruction of the diseased flock and compensation of the owner

ITEMS OF NOTE

1 Ornithosis is a disease of the psittacine birds pigeons and the domestic fowl and duck
2 Psittacosis is the disease found in wild parrots parrakeets parrotlets cockatoos and related species
3 The disease has appeared in endemic form in many bird breeding establishments and pet shops
4 Ornithosis is caused by a filtrable virus
5 Mice guinea pigs rabbits and monkeys are subject to experimental infection
6 Ornithosis of pigeons in the United States seems to be widespread
7 Man is highly susceptible to the virus of psittacine origin less so to the virus of parrot origin
8 The domestic fowl and duck apparently play a small role in the epidemiology of the disease
9 Control of the disease calls for an appreciation of the dangers inherent to contact with pet birds especially of unknown origin together with the creation of a bird industry free from psittacosis

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CHAPTER X

FOOT AND MOUTH DISEASE

FOOT-AND-MOUTH disease is an acute febrile affection caused by a filterable virus During the course of the disease characteristic vesicles develop on the mucous membranes of the mouth and on the skin of the interdigital spaces

Primarily it is a disease of cattle and other cloven footed animals secondarily other animals as well as man may become infected

Other names under which the disease has been known are aphthous fever epizootic aphtha infectious aphtha and eczema contagiosa

HISTORY

The history of foot and mouth disease seems to be shrouded in uncertainty For some centuries it has been known in Central Europe but it was ascribed to numerous causes such as climatic or meteorological conditions bad air excessive fatigue etc Its infectious nature was recognized in 1764 but until the development of bacteriology a century later the etiological factor or the mode of spread was not known Epidemics have recurred at frequent intervals in different parts of the world As an illustration of its severity in Central Europe in 1911 Mohler relates that 3 366 369 cattle 1 602 927 sheep 2 555 731 hogs and 53 674 goats were affected or approximately one out of every seven animals in that region

In the United States from 1850 to 1933 foot and mouth disease appeared in epidemic form among cattle on ten different occasions In 1870 an outbreak introduced from Scotland by way of Canada spread into New England and New York State but seems to have been arrested in a short time In 1880 the infection was discovered in two or three lots of imported cattle but the contagion was arrested before it could spread to other herds In 1884 the third outbreak appeared at Portland Maine but was soon under control All

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tine regulations automobiles were prohibited from passing into Arizona from California Cars and tourists accumulated at the border for several days until at one point more than 200 cars carrying 700 people were waiting Finally they were allowed to go on their way after thorough disinfection

The original infection in this epidemic was supposed to have come on a transport from the Orient with garbage used to feed hogs in California From its focus around San Francisco Bay the disease spread to sixteen counties in California within a period of six months requiring the destruction of more than 58 791 head of cattle

In September 1924 the disease appeared in Texas but was brought under control within 30 days by immediate and complete slaughter of 148 herds The source of the trouble is not known certainly except that it probably had no relation to the California outbreak It is thought that possibly it was brought in by members of crews from ships taking on cattle from infected foreign ports for food purposes The next year a recurrence appeared which was immediately suppressed with the slaughter of 153 infected herds and 848 exposed herds

The ninth outbreak of foot and mouth disease occurred in California from January to March 1929 and was limited to five herds of hogs The source of infection was infected garbage from a ship from South America Several new methods of control were used in this outbreak Frequent temperature readings were made of suspected animals for early diagnosis chicken wire was erected around infected premises to keep out roving dogs cats and poultry as well as unauthorized persons sodium hydroxide was used for the disinfection of clothing worn by inspectors

In April 1932 foot and mouth disease again appeared in Southern California involving thirty seven herds of hogs The source of infection was not certainly determined but was presumably infected garbage Within three weeks the outbreak was brought under control

In 1933 there was a small outbreak in hogs in San Diego which may have been a recrudescence of the 1932 infection

GEOGRAPHIC PREVALENCE

Foot and mouth disease has prevailed at different times in nearly all parts of the world in all climates In Europe it has become endemic breaking out from time to time with tremendous losses

especially in France Germany Switzerland, Italy and other central countries The isolation of Great Britain Denmark, Norway and Sweden has made possible a fairly successful control In Asia there have come reports from China Russia Japan and the Philippine Islands In South America it has appeared in years past in Brazil Argentina and Uruguay

In the United States the outbreaks reported above have occurred from Maine to California In each instance they have been quickly suppressed however so that the country may be said to be free of infection The same is true of Canada and Mexico

ANIMALS SUSCEPTIBLE

Cattle hogs sheep and goats are very susceptible to infection while the buffalo American bison camel chamois llama giraffe and antelope follow closely in order along with other cloven footed animals

Dogs cats and poultry show slight susceptibility but may become infected on occasion The Berlin Commission found the dog and cat refractory Olitsky found the horse refractory

Among the laboratory animals the guinea pig is the animal of choice for experimental purposes Some of the early investigators found guinea pigs refractory to infection and Hobmaier could pass the virus through them but a limited number of times before losing it It is now generally accepted that the guinea pig is quite susceptible to infection with the virus and once the disease becomes established in this animal it can be propagated indefinitely by passage from animal to animal Olitsky and Boez (3) passed the virus through 261 successive guinea pigs with no loss of virulence by injecting it intradermally into the foot pad The disease progresses rapidly in such animals but does not spread naturally from animal to animal

Rabbits and rats on the other hand are much less susceptible to infection than guinea pigs and the disease following successful inoculation is correspondingly less marked

THE ETIOLOGIC AGENT

The virus of foot and mouth disease is of historic interest Loeffler and Frosch (5) in 1897 showed that it would pass through clay filters so fine that ordinary bacteria were held back Thus was dem

onstrated for the first time the so called filterable viruses as a source of contagion for man and animals The virus may remain alive and active for 6 months if kept moist and cool at a temperature between 3 5 and 5 5 C and for 105 days when dried rapidly in a vacuum at room temperature On infected premises the virus remained active 283 days in one instance and 345 days in another (10) Heating at 55 C for 15 minutes destroys it It withstands bichloride of mercury 0 1 per cent or cresol 3 per cent for six hours It is quite resistant to certain chemical disinfectants as ether alcohol or chloroform but Olitsky has shown that this was because of a protective precipitation of protein around the molecule When an alkaline solution is used such as sodium hydrate in 1 or 2 per cent to prevent coagulation of the protein the virus is quickly destroyed

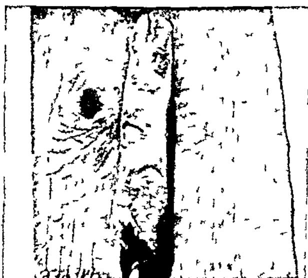
The virus of foot and mouth disease is about 10 millimicrons in size It has not been cultivated artificially Material diluted 10 000 000 times is still capable of infecting guinea pigs There are several types of the virus immunologically which do not protect against each other The French workers have reported two types A and O while the Germans have reported a third C

The virus of foot and mouth disease is closely related to the virus causing vesicular stomatitis in horses and to the virus causing vesicular exanthema of swine and can be differentiated only by certain immunologic and pathogenic properties All three viruses are experimentally infective for swine The virus of vesicular exanthema differs from the other two immunologically and in its failure to induce lesions in cattle it is infective for the horse experimentally The virus of vesicular stomatitis differs from that of foot and mouth disease immunologically and by its pathogenicity for the horse as well as by its lessened degree of virulence for cattle and guinea pigs

Traum (10) has drawn attention to the adaptation and predilection of these viruses for certain species The virus of foot and mouth disease in an outbreak in 1927 28 in Germany decreased and lost its virulence for cattle In 1920 in an outbreak of foot and mouth disease in sheep and goats in Germany the virus was only slightly infective for cattle and swine although usually the reverse is true In Argentina the virus of foot and mouth disease would not infect guinea pigs but would readily infect cattle The virus encountered in the 1932 outbreak in California among hogs did not infect cattle or guinea pigs but did infect horses

THE DISEASE IN ANIMALS

Foot and mouth disease is the most contagious infection known to veterinary science Cattle are very easily infected by a single exposure One incident is related in which an infected lost calf trying to find its mother spread the disease to twenty small dairy herds Instances have been reported however where infection was slow



United States Department of Agriculture

FIG 42 —Lesions on tongue in foot and mouth disease

to take place where uninfected cattle put into infected stalls or into contact with infected cattle did not become infected themselves (12)

The incubation period may range from eighteen hours to three weeks usually being from three to six days The disease first indicates itself by fever Two or three days later small blisters appear on the mucous membranes of the mouth Then the feet become swollen and tender and vesicles appear as in the mouth The animal becomes lame refuses to eat because of pain and if a milch cow almost dries up its flow of milk The death rate is small in this form of attack and the animal will regain its normal appetite in 10 to 20 days The full flow of milk is retarded for a long time however More malignant types of the disease attack the internal organs and quickly cause death or leave the animal permanently injured

Among young animals the death rate may be 60 to 80 per cent as a result of gastroenteritis or endocarditis

The vesicles which form in the course of the disease contain the virus in concentrated form When those in the mouth rupture the saliva becomes infected and thus infection is spread to manger and pasture food and water Virus from vesicles on the feet is trailed wherever the animal goes while that on the udder may contaminate the hands of persons coming in contact with the animal and thus be spread to other animals



United St t D p rtment of Agricult

Fig 43 —Lesions on hoofs in foot and mouth disease

Human carriers of the virus of foot and mouth disease may be responsible for a certain per cent of the cases among cattle Direct contact with infected animals is the most important factor while indirect contact follows closely

THE DISEASE IN MAN

Human infection with the virus of foot and mouth disease is probably rare There are a considerable number of cases reported in the literature *few of which have been verified by inoculation of* susceptible animals Trautwein in 1932 could find reference to only three human cases where contents of the bleb had been proven by animal experimentation to be foot and mouth disease virus

The comparative resistance of man to the virus is indicated by the experience in 1908 when smallpox vaccine virus infected with

foot and mouth disease virus was widely distributed in the United States with no human cases of the latter disease Similar instances have been reported from Norway and from Rumania no human cases occurring, although fatal infections could be induced in cattle and swine

Transmission of the virus through the milk from infected animals is possible and several unverified cases have been reported Law observed human infections from drinking infected milk in the 1870 epidemic in the United States while other supposed infections from a similar source were reported in the epidemics of 1902 1908 and 1914 Duglosz (13) has reported a case in Poland from infected milk

Infected cattle have been slaughtered and used for human consumption with no cases in man being reported (15)

Direct inoculation through the broken skin is possible Gins (6) records the case of Pape who contracted the disease through a wound on the hand caused by the breaking of a flask filled with vesicular contents Trautwein (11) reports the case of a caretaker who accidentally cut his finger while infecting cattle with foot and mouth disease virus a few days later developing symptoms of the disease that were verified by animal inoculation Duglosz describes a case where the patient injured his finger with a splinter from a butcher s block

An eye infection has been reported from Rumania (14)

The disease in man is usually very mild and there is a possibility that it may be overlooked The symptoms are fever vomiting painful swallowing sensation of heat and dryness of the mouth followed by an eruption of vesicles distributed over the mouth lips and tongue The hands may also be affected Headache pain in the back vertigo colic diarrhea and weakness accompany some cases Probably very seldom is the disease fatal

PREVENTION AND CONTROL

The control of foot and mouth disease in the United States is accomplished by the slaughter method All infected animals immediately upon diagnosis and all animals exposed to infection are slaughtered and disposed of by burning or burial Thus the greatest source of active virus is removed The premises and all materials that could possibly be contaminated with the virus are carefully cleaned and disinfected Test animals are used to prove the thor

oughness of the disinfection and the safety of the premises cattle and swine being allowed to feed and graze and otherwise come in contact with all portions of the premises that might have been infected by the virus A rigid quarantine around infected areas is maintained with precautions against unauthorized visitors A chicken wire fence prevents chickens dogs and other animals from wandering on and off infected premises spreading the virus The shoes and clothing of persons leaving the premises are disinfected with sodium hydroxide

In Europe and elsewhere the disease has become endemic and is difficult to eliminate Vaccines and serums have been used with varying degrees of success In Italy Rushmore (15) prepared vaccine after a modified Waldmann method obtaining no failures in 36 000 cattle vaccinated

Pasteurization of milk is a simple and effective safeguard for the public against infection Milk butter and cheese from infected or suspected areas should receive like treatment For those persons who must come into contact with infected animals as veterinarians farmers etc the ordinary precautions of personal hygiene will go far towards protecting them

ITEMS OF NOTE

The unique features of foot and mouth disease are several

1 It is the most highly contagious disease to which cattle may be exposed
2 It is not particularly infectious for man
3 The death rate in man is very low
4 The virus has certain similarities with that of vesicular stomatitis of horses and vesicular exanthema of swine
5 The eradication of foot and mouth disease has been accomplished in the United States only by the most drastic and complete destruction of infected and exposed herds
6 It can be said that in the United States foot and mouth disease does not exist either as an agricultural or public health problem

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CHAPTER XI

THE POX DISEASES OF MAN AND ANIMALS*

SMALLPOX or *variola* is a disease primarily of man It is ordinarily transmitted directly from man to man It can however be transmitted by inoculation to a variety of animal species in which the disease generally is quite mild and usually localized Rarely the infection is transmitted from smallpox patients to animals by natural contacts When smallpox virus becomes adapted to animals it generally loses much of its virulence for man and when carried back to man by inoculation the disease produced is mild and localized and is known as *vaccinia* Vaccinia confers immunity in man to smallpox and vaccination has long been used for protecting people against this dangerous and disfiguring malady

Diseases with skin eruptions similar to those of smallpox in man occur in cattle horses swine sheep goats rabbits and other mammals We also have pox diseases in birds but the manifestations are somewhat different from those in mammals Generally the animal poxes are naturally restricted to their own host species but experimentally most of those affecting mammals can be inoculated successfully into rabbits and some of them into other animal species In experimental animals the character of the lesions is practically alike irrespective of the original host species These facts have led many to believe that the pox diseases of man and other mammals at least have originated from a common stem and that the host specificity seen today is the result of adaptations to different hosts The relationship of the virus adapted to cattle (cowpox) to the one adapted to man (smallpox) is particularly interesting and important

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HISTORY OF SMALLPOX

The history of smallpox has been lost in prehistoric times Its original home is not known but the earliest records show that it prevailed in the Orient The first precise description of the disease was given by Rhazes an Arabian physician in the ninth century A D It is certain however that it had existed for several centuries before the Christian era in China The *pesta magna* described by Galen in the second century is believed to have been smallpox The disease was prevalent in the sixth century and it existed again among the crusaders who carried it from Asia Minor into the countries of western Europe The disease was a scourge in Europe during the middle ages and later During the 18th century it has been estimated that as many as 60 000 000 people died of it Most children contracted it and those who escaped it in childhood generally suffered from it later in life Numerous references in English literature indicate the fear and terror which it inspired in the popular mind Ben Jonson about 1600 wrote

> Envious and foule disease could there not be
> One beautie in an age and free from thee

Lord Macauley has given a powerful word picture of conditions about 1700

> The smallpox was always present filling the churchyard with corpses tormenting with constant fears all whom it had not stricken leaving on those whose lives it spared the hideous traces of its power turning the babe into a changeling at which the mother shuddered and making the eyes and cheeks of the betrothed maiden objects of horror to the lover

Smallpox was introduced into the Western Hemisphere by the Spaniards shortly after the continent had been discovered by Columbus There it proceeded to devastate the Indian population Catlin has estimated that at least 6 000 000 of them died with the disease prior to the time that the continent was heavily colonized by the white men Similar pictures of the disease have been presented from many other parts of the world

It was under conditions such as these that Edward Jenner was reared Jenner was a country doctor practicing in western England It was he who showed the way to change smallpox from the devastating disease that it had long been to the much milder one as we know it today In 1798 Jenner published a pamphlet entitled An

Inquiry into the Causes and Effects of the Variolae Vaccinae a Disease Discovered in Some of the Western Counties of England Particularly Gloucestershire and Known by the Name of the Cow Pox in which he showed that it was possible to protect people against smallpox by vaccinating them with lymph taken from the lesions of cowpox It seemed that it was common gossip at the time among country folk that an infection with the mild cowpox would give them protection against the deadly smallpox To determine whether this belief was correct Jenner on May 14 1796 collected lymph from the hand of Sarah Nelms a dairy maid affected with cowpox and transferred it to the arms of James Phipps an eight year old boy A typical take followed Six weeks later the boy was inoculated with smallpox He proved to be immune to it Such experiments were multiplied with the same results It was true that the mild cowpox would immunize to the virulent smallpox and the method soon was widely used for this purpose

Probably the first vaccinations in America were done by Waterhouse who in 1800 vaccinated his own son with cowpox lymph obtained from England dried upon threads In 1802 an experiment was conducted in Boston in which 19 boys were vaccinated Three months later twelve of them were infected with smallpox without result Two others not previously vaccinated developed the disease following inoculation with the same virulent material which had been used on the vaccinated boys These experiments did much to develop faith in vaccination as a means of controlling smallpox in America

THE ETIOLOGIC AGENTS

All of the pox diseases are caused by filtrable viruses They are characterized in mammals by the appearance of skin eruptions which begin as papules and later become pustules with characteristic umbilications in their centers Before the skin eruptions appear virus can be found in the blood and internal organs of persons suffering from either variola or vaccinia In the cells of the deeper layers of the corium of the affected skin in all pox diseases characteristic bodies may be found Those of smallpox were first described by Guarnieri (1) in 1892 and they were regarded by him as the cause of the disease In his honor they are now known as Guarnieri bodies They are relatively large and stain readily with tissue stains They lie in the cytoplasm of the affected cells The exact nature of these

bodies is still uncertain but they belong to a group of such structures found in many virus diseases, which are now known as *inclusion bodies* They cannot of themselves be the causative agent of smallpox, since the virus is filterable through Berkefeld filters whereas Guarnieri bodies are far too large to pass such filters

Structures similar to Guarnieri bodies are found in the pox lesions of all animals Some of them are given other names e g the Bollenger bodies of fowlpox but most of them are unnamed

In 1906 Paschen (2) described small bodies much smaller than the Guarnieri bodies in the lymph and infected epithelial cells of the lesions of vaccinia in children Paul inoculated the cornea of the eye of rabbits with suspensions of these bodies washed free of extraneous matter and produced characteristic pox lesions containing Guarnieri bodies These findings have been corroborated by many others These minute bodies are now known as Paschen bodies or elementary bodies Since purified suspensions readily produce pox and since they agglutinate in immune serum these bodies are now regarded as the virus elements They measure about 0 2 microns in diameter and readily pass through the coarser Berkefeld filters They are among the largest of the viruses according to Elford and Andrewes (4)

Similar elementary bodies have been found in the other pox diseases Those of fowlpox are known as Borrel bodies They have been thoroughly studied by Woodruff and Goodpasture (5) who found that they were resistant to tryptic digestion and thus could be freed from tissue elements by digesting the suspensions with artificial pancreatic juice Suspensions of such purified bodies readily produce fowlpox When the bodies are centrifuged out of suspension the supernatant fluid becomes innocuous These experiments strengthen the belief that these bodies actually constitute the virus of pox

Pox virus is destroyed by heating at 100°C for three minutes It is especially resistant to drying According to Paschen dried vaccine virus will remain viable for as long as 229 days It is resistant to many common disinfectants In 0 5 to 1 0 per cent phenol solution the virus remains alive for long periods Commercial vaccine virus is commonly preserved in 50 per cent glycerol solution plus a dye brilliant green since these agents have little effect on the virus but tend to restrain multiplication and eventually destroy any bacteria which may be present

Vaccine virus may be propagated indefinitely by serial passage

through rabbits which have been inoculated either on the cornea of *the eye or into the tissue of the testicle* Parker and Nye (6) cultivated the virus free of bacteria in tissue cultures of cells taken from the testes of the rabbit Rivers (7) cultivated vaccine virus in pure culture in minced chick embryo suspended in Tyrode s solution Goodpasture Woodruff and Buddingh (8) used the chorio allantoic membrane of the developing chick embryo for the same purpose By the use of these special technics the elementary bodies of vaccinia have been collected in large amounts for study and for the making of vaccine

THE ANIMAL POXES

Jenner believed that smallpox cowpox and an eruption occurring on the pasterns of horses which was known as grease were modified forms of the same disease Early in the 19th century observations were made in both Europe and America which indicated that cowpox and smallpox were identical diseases except that one occurred in cattle and the other in man The Lyons Commission in France (9) about 1864 produced lesions in cows identical with those of cowpox by inoculating them with material from cases of human smallpox Freyer (10) not only produced typical vaccinia in cows by the use of smallpox material but he used lymph from these animals for successful vaccination of people These results have been confirmed by many and are now accepted facts The virus of smallpox can readily be converted into the virus of vaccinia by animal passage None has been able to change the virus of vaccinia into that of smallpox however

Methods of artificial culture of vaccinia virus have made it possible to collect large numbers of elementary bodies in a relatively pure state With such suspensions it is possible to conduct most of the serological tests that are used for establishing the identity of strains of bacteria Agglutinins lysins and complement fixing bodies have been produced which react with the elementary bodies in the same way that such antibodies react with bacteria These antibodies react with the elementary bodies of variola and vaccinia alike Therefore it can be regarded that a close relationship if not actual identity has been established between the viruses of smallpox and cowpox Similar relationships may exist between the viruses of smallpox and those of other pox diseases but the proof has not been supplied

Cowpox and Pseudo Cowpox (Paravaccinia)—The literature on naturally occurring cowpox is conflicting and confusing It seems likely that there are at least two entities perhaps more that are included in the clinical syndrome One of these is the true cowpox already discussed which is immunologically closely related to small pox in man This infection can be transmitted easily from cow to cow by inoculation and recovered animals are thereafter highly re sistant to inoculation with vaccine virus This is the classical cowpox of Jenner—the one that conveyed smallpox resistance to the milkers This disease apparently was much more common in Europe and America a century ago than it is at present Since smallpox was also more prevalent then than now it seems likely that the bovine dis ease had its reservoir in the human family In more recent times there have been a number of reports of cowpox outbreaks in dairy herds as a result of infection from recently vaccinated milkers Boer ner (11) has reported such an outbreak in Pennsylvania in which the infection introduced in this way spread through an entire herd and a number of persons were infected secondarily Another such outbreak was reported by Sayer and Amoss (12) in New York in which two herds were infected by the same recently vaccinated milker and in which additional milking personnel in both herds be came infected There have been other reports both from this coun try and abroad and additional instances are known which have never been reported in the literature These experiences teach the lesson that *recently vaccinated persons should never be permitted to work as milkers on dairy farms until their vaccine reactions are well healed*

A disease which is universally known as cowpox is common in all dairy districts in this country and in Europe as well The lesions occur for the most part on the teats but often on the skin surface of the udder itself They begin as papules which change to vesicles and finally pustules The vesicles often coalesce and those on the teats usually rupture through the friction of the milking process leav ing raw surfaces These become covered with dry crusts Healing is delayed in milking animals by the breaking off of these scabs in milking When such lesions occur near the end of the teats they often pave the way for bacterial invasion of the udder and the pro duction of cases of suppurative mastitis If mastitis does not result the general health of the animals is not noticeably affected but the

soreness of the teats makes them difficult to milk The disease usu ally spreads through the herd obviously by the milking process since non lactating animals usually escape infection

This disease deserves more study than has been given it so far For several reasons it seems obvious that it is not true cowpox For one thing infection of the people who handle and milk these ani mals very seldom occurs and when it does the clinical picture is not that described by Jenner and by others More convincing per haps is the fact shown by Christen (13) in Switzerland and con firmed by Hester Boley and Graham (14) and Gibbons (15) in this country that vaccine virus neither prevents this disease nor does this disease render the animals insusceptible to subsequent vaccina tion Also Christen and Hester Boley and Graham were not suc cessful in transmitting this disease by inoculation to normal cattle This does not accord with the experience of many who worked with the genuine cowpox in past years The commonly occurring disease which we call cowpox today obviously is not cowpox or it is a pox strain which has become more closely adapted to cattle and less adapted to man than those of earlier days In the German literature the disease has been called para vaccinia English and American authors have referred to it as pseudo cowpox Its relation to an affliction of man will be discussed in the next chapter (see chapter XII)

THE POXES OF ANIMALS OTHER THAN CATTLE

Horsepox —This disease also known as contagious pustular stoma titis of horses now seems to be rare in Europe and there are no records of its occurrence in North America According to Zwick (16) who investigated the disease thoroughly the causative agent is the virus of vaccinia The disease is characterized by papules vesicles and pustules which appear on the mucous membrane of the mouth and occasionally on the skin

Sheeppox —According to reports this disease often is quite prev alent and destructive in south eastern Europe It has not been re ported in North America The virus can easily be transmitted to other sheep but is not easily transmitted to rabbits or other species Inclusion bodies resembling those seen in vaccinia are found in the affected epithelial cells

Similar in many respects to sheeppox except that it is usually

localized in the mucous membrane of the lips is the disease known as sore mouth or contagious ecthyma This is a very common disease on the sheep ranges of our western states and many farm flocks in other parts of the country frequently become infected (see chapter XIII)

Swinepox—This is a rather common disease in this country and abroad In general it is not considered to be serious but there are those who feel that its importance is greater than is generally thought The lesions are usually found on the under parts of the body and it is known that the common hog louse plays an important role in the spread of the disease As in cattle it is obvious that there are two different diseases masquerading under the name of pox in swine One of these is the true pox associated with a virus which is closely related to vaccinia and the other is caused by a disrelated virus The true pox occurs in Europe but there are no authentic reports of its existence in America The so called swinepox of this country *cannot be transmitted to animals other* than swine according to McNutt Murray, and Purwin (18) Schwarte and Biester (19), and Shope (20) and therefore must be regarded as pseudo pox There are no records of American swinepox having been transmitted to man

Fowlpox—*The pox diseases of birds (chickens pigeons* turkeys canaries etc) are caused by viruses which are not closely related to vaccinia immunologically Neither do the lesions resemble those of true pox in mammals The lesions are seen most frequently around the head but also occur on the feathered portions of the body They *consist generally of epithelial thickenings rather than of* vesicles and pustules as in mammals In the affected cells however there are bodies which resemble the Guarnieri and Paschen bodies of vaccinia The bird poxes usually affect only the species in which they originate but a certain amount of cross immunity can be produced *by inoculation thus pigeonpox virus is used* practically for immunizing laying hens against chickenpox Vaccinia virus does not easily take on birds and does not immunize against the bird viruses and vice versa

PREPARATION AND USE OF VACCINE VIRUS

Smallpox vaccine has been produced on a commercial scale longer than any other of the biologic products used for prophylaxis Until

quite recently all vaccine was produced by propagating the virus on the scarified skins of calves and most of it is still made in this way Animals with white skins and weighing up to 250 pounds are preferred They are carefully examined for any abnormalities before being purchased for vaccine manufacture and this includes tests for tuberculosis and brucellosis They are then kept in quarantine for observation for a week or more After the vaccine is harvested the animals are destroyed and subjected to a postmortem examination as a final check on their health before the pulp is processed for use

It appears that most if not all vaccine made in this country is manufactured from the same strain of virus which probably originated from Jenner s stock All of it is produced under license from the National Institute of Health which under law has the responsibility of setting up regulations for its production just as for all other biological products intended for use on man and which go into interstate trade

From time to time all manufacturers pass their virus strain through rabbits or through man since otherwise it tends to lose its effectiveness as an immunizing agent Except for this the strain is maintained constantly by passinge through calves For vaccine production the hair is clipped and the animal thoroughly washed It is then fastened to an operating table which gives good exposure of the abdomen and the inner aspect of the thighs and these areas are shaved and thoroughly scrubbed Sterile water sterile soap and sterile brushes are used for this process When the area is ready inoculation is done with a metal scarifier which makes superficial longitudinal scratches about 0 5 to 1 0 cm apart No blood is drawn The "seed pulp" which may have come from a rabbit or from another calf is then applied and rubbed in with a spreader After the pulp has dried on the skin the animal is released from the table and returned to its stall No dressing is applied to the scarified area The animal is fed as usual and is allowed to lie down at will The stall is kept scrupulously clean Some manufacturers spray the scarified area daily with a 1 1000 aqueous solution of brilliant green This helps to restrain bacterial growth but does not affect development of the virus

The vaccine pulp is collected about the 6th or 7th day After the whole area has been carefully washed with sterile water and dried with sterile towels the dried crusts are removed and discarded and the pulpy material lying underneath is collected with a curette and

placed in sterile bottles The calf is anaesthetized during this process and destroyed immediately afterward The vaccine pulp contains not only the vaccinia virus but a considerable number of bacteria some of which may be pathogenic

These extraneous organisms are destroyed by the addition of glycerin 50 per cent and carbolic acid 1 0 per cent with storage at a temperature of about 5°F Investigations carried on in the New York City Health Department (21) have shown that brilliant green in a final concentration of 1 10 000 does not affect the vaccine virus but greatly hastens the destruction of other organisms

Tests for potency and purity are made before the material is used The vaccine must be free from tetanus bacilli must not contain more than 50 organisms per vaccination and must give typical takes on a rabbit when diluted 1 1 000 up to 1 30 000 as compared with vaccine of known strength

In years past vaccine virus was dried on bone points" or used in bulk Regulations now prohibit any distribution except in sealed capillary glass tubes

Work by Rivers (7) and by Goodpasture and his co workers (22) with the cultivation of vaccine virus in pure culture added new possibilities to the methods of vaccination The absence of contaminating organisms permits the omission of glycerin and other substances for the destruction of the contaminants resulting in a much increased period of potency for the vaccine virus Not only have takes been obtained with the pure culture virus in a much higher percentage of cases than with glycerinated virus but intradermal injections also are possible whereby no scars are left

EFFICACY OF VACCINE VIRUS

The protective power of vaccine virus has been demonstrated on numerous instances In Sweden during the twenty eight years before vaccination (1774 1801) the annual death rate from smallpox per million population averaged 2 050 in the forty years following vaccination, smallpox deaths averaged only 158

Wherever a determined effort has been made to vaccinate a large part of the population smallpox has almost disappeared when laxity begins to prevail smallpox again becomes prevalent This is strikingly illustrated in England and in the Philippine Islands

In England and Wales smallpox vaccination was voluntary prior to 1871 In that year vaccination of infants became compulsory

Following are the deaths from smallpox as given by White

1867 1876	52,218
1877 1886	18 026
1887 1896	5 092
1897 1906	4 761
1907 1916	139
1917 1926	138

Even without a subsequent vaccination in childhood smallpox deaths became very infrequent In 1898 however a "conscience clause" was introduced into the law which exempted those who should claim conscientious scruples against the practice It was only necessary for a "crop" of susceptible individuals to grow up there fore to have smallpox become again prevalent

Beginning with 1922 a very mild type of smallpox became preva lent so called variola minor It increased to a peak in four or five years and then declined Whether the mild disease with a low death rate is an attenuated form of hemorrhagic smallpox is not entirely proved If this is true the question arises whether it will revert to the severe type In England in 1934 the increased death rate was due to the severe type In other places hemorrhagic smallpox has suddenly appeared in the midst of a mild epidemic

In the Philippine Islands previous to the American occupation 40 000 deaths occurred annually from smallpox When the Ameri cans introduced compulsory vaccination the disease disappeared wherever vaccination was applied In the provinces surrounding Manila the deaths fell from 6 000 annually to not one For seven years prior to 1914 there was not a single death in Manila from smallpox Then laxity began to prevail with a consequent increase in cases and deaths These were confined in 93 per cent of the in stances to the unvaccinated however Only by resumption of com pulsory vaccination was the disease again controlled

In the United States between 30 000 and 60 000 cases of smallpox occur annually In most states vaccination is voluntary In Massa chusetts children are required to be vaccinated before entering pub lic schools The average annual case rate per 100 000 population for the years 1921 26 was only 0 3 while for states where such vaccina tion is not required it was very high for the same period—California 104 1 Minnesota 112 7 Washington State 152 1

The figures for smallpox in California illustrate what happens in

a population in which systematic vaccination is opposed or indifferently supported In such areas, smallpox tends to concentrate its attack upon children of school age In 1929 39 per cent of the cases in California occurred among such children the case rate per 100 000 in that State was nearly three times as high as for the population as a whole Smallpox under such conditions seems to occur in waves in California in six year periods

Between major outbreaks there is the ebb and flow movement of the disease attacking those among the unvaccinated who somehow or other escaped the disease during major invasions These cases keep the reservoir of infection going Imported cases often of the virulent hemorrhagic type add to the reservoir

Certain criticisms have been advanced against vaccination One is that it spreads syphilis This was possible and probable under the old method of transferring scabs directly from arm to arm under the present procedure of manufacturing vaccine virus it is impossible Another is that it is responsible for tetanus In 1903 Rosenau (23) showed that some of the vaccine virus offered for sale in the United States contained tetanus spores In 1917 McCoy and Bengston (24) demonstrated the presence of tetanus organisms on bone point scarifiers which were at that time in use for performing vaccinations Regulations at the present time are sufficiently stringent to prevent the distribution of vaccine virus contaminated with tetanus spores Armstrong (25) has studied post vaccination tetanus occurring in thirty two states in this country between 1914 and 1928 He found that dressings bunion pads shields and the like were responsible for the few cases of tetanus that developed (26) Recent methods of vaccination recommended by the United States Public Health Service absolutely avoid all dangers of tetanus infection

Post vaccinal encephalitis has appeared in some areas Factors causing the trouble are obscure and require additional studies Control seems to call for a virus without predilection for nervous tissue —a matter that may be solved by the use of pure culture vaccines A study of sixty years of vaccination in Germany would indicate that post vaccinal encephalitis regrettable as it may be does not justify the weakening of compulsory vaccination laws (27)

Eczema vaccination is a rare condition but nevertheless grave when it occurs resulting in blindness or death (28) Children with eczema may develop a generalized vaccinia from their own vaccina

tion or from infection by other recently vaccinated members of the family Control calls for a careful inquiry concerning eczema in the family and for protection of vaccinated areas so that the lymph may not be passed to other areas (29)

ITEMS OF NOTE

1 Smallpox of man and the pox diseases of several of the lower animals are definitely related This is especially true of the disease in cattle
2 Smallpox virus passed through cattle by natural contact or artificial inoculation becomes weakened for man and can be used for preventive inoculation This is the vaccine (Latin vacca = calf) virus used for vaccination
3 Vaccine virus has been proven by more than a century of experience to be efficient in suppressing outbreaks of smallpox and in preventing their occurrence
4 Present governmental regulations insure that vaccine virus is a harmless product for use on man

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CHAPTER XII

MILKER S NODULES*

Two kinds of lesions occur on persons who have a history of having associated with cattle suffering from a skin affection involving the udder and teats which is commonly diagnosed as cowpox Both types usually involve the hands and forearms of milkers suggesting that they are infections contracted by direct contact with the lesions of the cows Frequently if not always the lesions appear where there have been abrasions of the skin

One of these types develops in the form of discrete usually multiple papules which progress through vesicular and pustular stages to crusts which finally fall off leaving a healed surface These lesions are typical of vaccinia and they induce immunity to variola or smallpox as was first shown by Edward Jenner (1) Such lesions are described and illustrated in many of the earlier textbooks and one thus gains the impression that they were not uncommon in early times Such lesions have not been reported in this country in many years and Taylor (2) says that they are rare in England today although quite common many years ago

This infection may be regarded as typical vaccinia contracted from cows suffering from true cowpox Since it appears that true cowpox is now a rare disease in countries where smallpox is under good control (see chapter XI) it is not surprising that the human counterpart also has become rare

The second syndrome in man associated with "cowpox in cattle is known under the name of milker s nodules or milker s warts These lesions occur on the hands of milkers and usually are not numerous In most instances only one or two occur however Groth (3) saw a case in a German milkmaid in which there were 40 on one hand and 20 on the other Milker s nodules begin as papules sur

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rounded by erythematous areas in from 5 to 7 days after exposure They gradually enlarge into firm, elastic, bluish red nodules from one to two centimeters in diameter *Usually they are quite painless* Frequently they induce an itching sensation Sometimes there is slight swelling of the axillary lymph nodes After having attained full development the nodules are semiglobular with a slight central depression in their centers Gradually they tend to flatten If the grayish epithelial covering is broken the mass of the nodule is seen to consist of highly vascular granulation tissue The nodules flatten as healing progresses and the granulation tissue is absorbed From four to six weeks are required for involution to become complete No scars are left Bonnevie (4) in Denmark and Brants (5) in Latvia describe secondary efflorescences on other parts of the body When these occur they appear well after the primary nodules have developed and disappear within one week They appear as papules macules or urticarial wheals It is believed that they are of allergic or toxic origin

PREVALENCE

Milker s nodules have been described by a number of European workers representing a number of different countries an indication that the condition is quite widespread The only description of them in the United States is that of Becker (6) It is clear that the disease in man nowhere is as frequent as the corresponding disease in cows with which it is believed to be associated an indication that man is not highly susceptible to this infection or that peculiar conditions are required for transmission

THE CAUSE OF MILKER S NODULES

The relationship of these lesions to pox or pox like lesions in cattle is clear It is not so clear however whether the nodules are the result of the virus of true cowpox or of a pseudo pox producing agent

In Germany Schultz Seifried and Schaaf (7) produced pox like lesions on a calf by inoculating it with material from what they considered to be a milker s nodule From this calf they obtained a virus which caused infection when inoculated into other animal species including the rabbit In the cornea of the rabbit Guarnieri bodies were produced *After recovery from the inoculations the* animals proved refractory to reinoculations with the same virus and with vaccinia virus as well They thus proved that they were work

ing with a virus identical with or at least very closely related to that of cowpox They believed that this virus was the cause of the milker s nodules which the Germans call Steinpocken Warzen pocken or Spitzpocken " The question raised about the work of this group is whether the original material consisted of typical milk er s nodules several believe that they were not

Bonnevie quotes the experiences of Dolgov and Morosov (8) which are enlightening These workers failed to infect rabbits but succeeded in reproducing the disease in cattle and sheep using human material for inoculation Of interest is an outbreak of what was regarded as milker s warts in a slaughter house in Odessa Forty seven of the 300 employes developed the disease Only four of this group had milked cows but all of them had handled cows sheep and swine on which pox papules occurred In this case they were successful in infecting a number of animals and also several persons who had been vaccinated shortly previously and were immune to vaccinia As a result of this experience the authors concluded that the causative agent was a virus but was not the virus of cowpox They believed that it might be identical with the paravaccinia virus of Lipschutz Stark and co-workers (9) conclude as a result of their experience that the infective agent in these cases of atypical animal pox and milker s warts is a variola virus which has been altered in its biological properties by continued parasitism in foreign hosts Two of the patients described by Becker in the United States were vaccinated after recovery from an attack of milker s nodules with typical takes an indication that the nodules had not induced im munity to vaccine virus

Additional evidence that this disease in man is not related to the virus of cowpox has been obtained through studies made on the asso ciated condition in the cows Christen (10) in Switzerland on the basis of extensive work concludes that the common udder pox which prevails in that country is not true cowpox This conclusion was based upon the fact that the disease did not respond to vaccina tion with vaccinia virus and that recovered animals did not develop any immunity to vaccinia virus By contrast he found that true cow pox which he studied in one herd that had been accidentally in fected by a recently vaccinated milker did respond promptly to vaccination Numerous attempts to transmit the common udder pox failed a situation which he did not understand inasmuch as the natural disease was clearly quite contagious

Bonnevie (4) had the opportunity to check the immunity to vaccine virus of one of the cows which had been the source of a nodule infection in a milker The animal was supposed to have suffered from cowpox yet he was able to obtain a typical take with vaccine virus Hester Boley and Graham (11) in the United States studied the disease in cattle They were unable to produce the typical disease in other cattle or to obtain infection in rabbits Furthermore they were able to show that animals that had recovered from so-called cowpox gave typical reactions to vaccine virus Animals that had recovered from vaccination with vaccine virus could not be successfully revaccinated Also they were not successful in halting natural outbreaks of the disease in cattle by vaccinating them with vaccine virus Gibbons (12) also found that vaccination was not effective in halting the bovine disease Hardenbrook (13) continuing the work of the Illinois group confirmed the earlier work that the cattle disease was not related to vaccinia He has isolated an unidentified species of *Actinomyces* from early lesions of the disease with which he was successful in producing vesicular lesions on the udder of cattle These lesions do not resemble the natural lesions however hence further work is necessary to show the relationship if any between the fungus and this disease

The situation with respect to the etiology of the so called cowpox or udder pox of cattle which is a relatively common disease in this country and abroad and the rather uncommon human disease known as milkers nodules which is associated with it is uncertain *at present The bulk of the evidence indicates that these conditions* are not due to cowpox virus The difficulty which most workers have experienced in transmitting these infections to other individuals suggests that they may not even be induced by a virus Further work *is necessary to clarify the situation*

ITEMS OF NOTE

1 Milkers nodules or milkers warts occur in most instances in persons who have milked cows *suffering from a disease* which is commonly called cowpox
2 The condition in the cows associated with the human disease apparently is not true cowpox and there is much evidence that the human disease likewise *is not cowpox or vaccinia*
3 The causative agent of the cattle and human diseases is believed to be identical but its nature at present is unknown

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CHAPTER XIII

CONTAGIOUS ECTHYMA OF SHEEP

(Sore Mouth of Sheep)

CONTAGIOUS ecthyma of sheep (sore mouth of sheep contagious pustular dermatitis) is a communicable disease of sheep and goats caused by a filtrable virus Man is infected at rather infrequent intervals

GEOGRAPHIC DISTRIBUTION

The disease is probably of worldwide distribution In the United States it has been reported from many sheep raising areas of the west in the eastern states sporadic cases are encountered

SEASONAL PREVALENCE

The disease in the United States is most prevalent during the spring and early summer months This coincides with the period when young lambs are susceptible Later in the year they have attained an immunity and few cases appear

THE ETIOLOGIC AGENT

The etiologic agent is a filtrable virus It remains viable in scabs from lesions for many months when kept dry and cold It survives winter temperature in the soil of pasturelands and infects new lambs in the spring

ANIMALS SUSCEPTIBLE

Contagious ecthyma is a disease of sheep and goats It has been reported in no other domestic or wild animals

THE DISEASE IN SHEEP

Contagious ecthyma is a common disease of lambs While it may occur in very young animals it is more prevalent in lambs four to

six months old (4) Older sheep are immune The infection makes itself apparent first as whitish spots on the buccal mucosa These tend to grow and enlarge until they coalesce forming a false membrane If this is pulled off it leaves a bleeding eroded area if it is allowed to stay on it forms a heavy scab which eventually falls off leaving no scar During the course of the disease which lasts about one month lambs are unable to eat Hence there is malnutrition stunting and sometimes death from starvation

Fatalities are not great except in very young lambs (which are less often infected) or in cases complicated by other infections March and Tunnicliff (4) in Montana found that lesions superimposed with infection by *Actinomyces necrophorus* were much more serious Thorp (6) reported serious losses by death from this cause Boughton and Hardy (5) in Texas reported cases of contagious ecthyma which were invaded by larvae of the flesh fly *Cochliomyia americana* resulting in many fatalities

Animals which have recovered from the disease are immune

THE DISEASE IN MAN

According to Schmidt and Hardy (1) the possibility of transmission of sore mouth to man was suggested by Williams of Belgium Transmission of the disease to shepherds with the occurrence of stomatitis with vesicles on the gums tongue cheek and lips" was reported by Hatziolos of Greece Schmidt and Hardy in Texas encountered two similar instances but lacked proof of the relationship to the virus affecting sheep and goats

Brandenburg (2) reported an outbreak of lip and leg ulcer in North Dakota where two men who were treating the animals developed lesions on the hands and arms to the elbow and on the legs to the knees Large lentil like nodules appeared which were slightly painful and which smarted and itched if they were pressed upon or irritated in any way The neighboring lymph glands were swollen

Newson and Cross (3) relate the experience of a sheep feeder and his two helpers who treated a large band of sheep for sore mouth requiring three days to finish the task In removing cockleburs from the wool the workers irritated the skin on their hands Four days later there appeared on the hands of the feeder several large vesicles the larger ones being composed of several small compartments They were surrounded with a reddened zone and moderate swelling Lymph glands in the armpits were swollen with considerable pain

The lesions when opened emitted a thin limpid fluid Both helpers were afflicted with similar lesions

Fluid from one of the lesions on the hand was rubbed into a scratch on the inside of the thigh of a lamb Five days later there was considerable reddening around the scratch then a pustule along its entire length which attained its maximum development eleven days after inoculation Another lamb inoculated in the same manner developed vesicles in four days

The prevalence of human infections is probably small The disease in lambs is very widespread and quite common yet reports of man being infected are rare Possibly the lesions produced by the cockleburs in the cases of Newson and Cross had some effect The feeder in that instance had been associated fifteen years with infected animals without contracting the trouble

The duration of the disease in man is about three weeks with uneventful recovery

PREVENTION AND CONTROL

Pastures and premises once infected with the virus of contagious ecthyma remain in that condition for a long period of time resulting in new infections that are difficult to control

Boughton and Hardy (5) have reported a vaccine that is used to immunize young lambs Dried scabs from lesions are ground and suspended in fifty per cent glycerin one part scab to 100 parts solution A drop of this is applied and rubbed into a scratch on the skin inside the flank A small vesicle appears developing into a pustule and then a scab The lamb develops a permanent immunity without the usual manifestations of the disease unless the animal nibbles at the lesion and infects the lips In the small percentage of such instances the disease runs a much milder course than usual

In man the disease is so rare and so mild that the ordinary precautions of hygiene are sufficient

ITEMS OF NOTE

1 Contagious ecthyma of sheep is probably widespread over the world
2 Sheep and goats are the only susceptible animals
3 The etiologic agent is a filtrable virus
4 Man is infected only at rare intervals and the course of the disease is mild
5 Lambs and kids may be protected by vaccination

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CHAPTER XIV

ARTHROPOD BORNE ENCEPHALITIDES

THE arthropod borne encephalitides form a group of diseases caused by closely related viruses Birds are the natural hosts for most types though other animals are also implicated Mosquitoes and ticks are the usual vectors

The group * includes the following types (and probably others not yet sufficiently identified)

St Louis type encephalitis
Western type equine encephalomyelitis
Eastern type equine encephalomyelitis
Venezuelan type equine encephalomyelitis
Japanese B type encephalitis
Russian autumn fever
Russian spring summer fever
Louping ill

HISTORY

Equine encephalomyelitis has probably prevailed in the United States for many years being confused with various other maladies In 1854 a disease of horses in Boston was described the symptoms being similar to what is now known as the eastern type of equine encephalomyelitis (35) The malady was first reported as a separate entity by Meyer Haring and Howitt (1) when they described an epidemic of horses and mules in the San Joaquin Valley California that occurred in 1930 and again in 1931 These investigators not

* Type A encephalitis (Vienna type Economo type) occurs only in man and is not arthropod borne Australian X disease similarly lacks an animal host or insect vector Other viruses cause encephalitis in animals but have never been encountered in man Borna disease is an encephalomyelitis of horses and sometimes of sheep occurring in Saxony Porcine encephalomyelitis has been reported from Czechoslovakia Avian encephalomyelitis or epidemic tremor is a disease of young chicks in New England Encephalomyelitis of foxes (formerly confused with canine distemper) causes serious losses in fox farms in the United States

only isolated the virus but called attention to the possibility of human infections During the next few years the disease was reported in horses in many western states In the summer of 1933 a similar condition developed in Virginia Delaware Maryland and New Jersey Ten Broeck and Merrill (36) showed that the infecting agent differed serologically from the western type of the disease but was in most other respects quite similar In 1938 the eastern type of equine encephalomyelitis appeared in Massachusetts

In 1938 Beck and Wyckoff (2) differentiated the Venezuelan strain of encephalomyelitis as a type immunologically distinct from the North American types

The St Louis type of encephalitis made a sudden and explosive appearance in the metropolitan area of St Louis in the summer of 1933 (3) The year before there was an epidemic in Paris Illinois and other outbreaks were encountered in the years that followed The disease seems to be widespread over the United States Serologic evidence of its presence was presented in California in 1937 1938 (4) Other reports came from Arizona (5) in 1941 and from Washington the same year (6) In 1944 the virus was isolated from mosquitoes in California (7)

Japanese B encephalitis was first reported from Japan in 1871 Other outbreaks appeared in the years that followed but they attracted little attention until 1924 when there was an epidemic involving more than 6000 persons with 3 797 deaths In 1940 it was shown that mosquitoes acted as vectors

Russian autumn encephalitis encountered by Smorodintseff in Siberia in 1940 seems to be identical with Japanese B encephalitis

Louping ill has been known for many years in England and Scotland In 1807 Duncan described the malady In 1900 the Louping Ill Committee of the English Board of Agriculture (8) studied the problem Investigations conducted by numerous workers added much to the knowledge concerning the disease but failed to demonstrate the causative agent In 1930 Pool Brownlee and Wilson (9) succeeded in passing the disease from sheep to sheep and from sheep to pigs and showed that a filterable virus was responsible for the symptoms In 1932 Gordon Brownlee Wilson and McLeod (10) proved that ticks were the vectors of transmission

Russian spring summer encephalitis was studied by Russian investigators (11) who reported in 1938 the isolation of a virus from human cases in the European Soviet States Casals and Webster

(12) demonstrated that this virus is identical with that of louping ill from England The spring summer virus of Siberia seems to be different (7)

Other outbreaks of encephalitis have occurred which probably belong to this group, although they have varied in some details Woodland and Smith (13) described an outbreak in Texas and Hammon has encountered similiar instances in Washington and California where the etiology was obscure Bugher reported cases in Colombia which were difficult to identify It would seem that there are a large number of these arthropod borne neurotropic viruses of man and animals

GEOGRAPHIC DISTRIBUTION

The several types of virus causing equine encephalomyelitis are widespread over Europe North America and South America The eastern type of virus has been confined largely to the east coast of the United States from Florida to Massachusetts Kelser (14) in 1938 reported an infection of the eastern type in an army horse in Panama the animal having been brought from Nebraska several years previously Randall and Eichhorn in 1941 encountered a small outbreak in Texas the disease being of the eastern type In 1944 the eastern type was reported in horses in Brazil This type has been found also in Ontario Canada near the Great Lakes

The western type has prevailed in the United States from California to the Appalachian range in Saskatchewan and Manitoba Canada in Argentina Peru and Chile

The Venezuelan type has been confined to Venezuela Colombia and Trinidad

The St Louis type which resembles the western type in many respects is found largely in areas where the western type exists Antibodies to the virus are present in blood serum of normal persons and convalescent patients in many parts of the United States and in Central Africa (15)

Japanese B encephalitis has been reported from Japan Formosa Ryukyu Islands eastern China and Siberia (Russian autumn encephalitis) Positive serologic tests for this type of fever have been reported by Sabin in Cincinnati (16)

Louping ill of sheep is limited to certain areas of the border countries of England and Scotland and in the Western Highlands

Russian spring summer encephalitis has been reported in the European Soviet States as well as the Far Eastern area

SEASONAL PREVALENCE

The seasonal prevalence of the mosquito borne types of encephalitis is the late summer and early fall corresponding to the period of mosquito activity Cases at other times of the year may occur sporadically due to an unknown method of transmission Large epidemics never have occurred at times other than summer and fall

In England louping ill in sheep corresponds to the feeding period of ticks Most of the cases occur between the middle of March and the middle of May

In Russia tick borne encephalitis likewise occurs during the period of tick activity the season of greatest incidence being the end of May and the beginning of June

THE ETIOLOGIC AGENTS

The several viruses are immunologically distinct but in other ways quite similar The size is about 20 to 35 millimicrons In brain tissue preserved in 50 per cent glycerin they remain infective for one year in a dried condition they lose virulence more readily in a frozen condition a 20 per cent suspension was infective for thirteen months The viruses are destroyed by heat at 70°C in 10 minutes in suspensions and at 60 C for 10 minutes in filtrates they do not lose virulence at 56 C for 30 minutes The viruses are more sensitive to acid than to alkaline reactions losing viability below pH 5 5 but retaining it at pH 9 2 The viruses withstand phenol in 1 0 per cent solution for one month they withstand cresol solutions merthiolate mercuric chloride and chlorinated lime for considerable lengths of time They can not be cultivated in ordinary laboratory media but will grow in chick embryos

ARTHROPOD VECTORS

A large number of mosquitoes have been implicated in the transmission of the encephalitis viruses while ticks assassin bugs and mites also are of more or less importance (table 27)

Mosquitoes involved in the transmission of St Louis virus include *Culex tarsalis Culex pipiens Culex tritaeniorhynchus Aedes dorsalis Aedes lateralis Aedes taeniorhynchus Aedes vexans* and

Aedes nigromaculis The dog tick *Dermacentor variabilis* is capable of transmitting the virus experimentally and passing the infection through the egg to the new generation (17)

Table 27—ARTHROPOD VECTORS OF ENCEPHALITIDES VIRUS

	Western Virus	Eastern Virus	Venezuelan Virus	St Louis Virus	Japanese B Virus	Russian Autumn Virus	Louping Ill	Russian Spring-Summer Virus
Mosquitoes								
Aedes aegypti	+	+						
Aedes albopictus	+			+	+*	+		
Aedes cantator	+	+						
Aedes atropalpus		+						
Aedes dorsalis	+			+				
Aedes japonicus					+	+		
Aedes lateralis				+				
Aedes nigromaculis	+			+				
Aedes taeniorhynchus	+	+	+	+				
Aedes vexans	+	+		+				
Aedes sollicitans	+	+						
Aedes togoi					+*	+		
Aedes triseriatus		+						
Anopheles maculipennis freeborni	+							
Anopheles neomaculipalpus	+		+					
Culex pipiens	+			+				
Culex pipiens var *pallens*	+	+		+	+	+		
Culex stigmatosoma	+							
Culex tarsalis	+			+				
Culex tritaeniorhynchus		+		+	+	+		
Culiseta incidens	+							
Culiseta inornata	+							
Mansonia titillans			+					
Ticks								
Dermacentor andersoni	+							
Dermacentor silvarum								+
Dermacentor variabilis				+				
Haemaphysalis concinna								+*
Ixodes persulcatus								+
Ixodes ricinus							+	
Assassin bug								
Triatoma sanguisuga	+							
Mite								
Dermanyssus gallinae	+			+				

* Laboratory vector but not proven to be a vector in nature

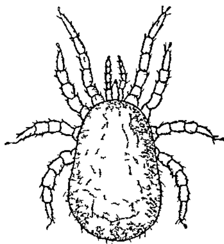
Japanese B virus is transmitted by *Culex pipiens* var *pallens* *Culex tritaeniorhynchus* *Aedes togoi* *Aedes albopictus* and others Hammon and Reeves (7) draw attention to the potential danger from this virus in the United States They demonstrated that at least six species of mosquitoes in California were capable of trans

mitting Japanese B virus experimentally If the virus was once introduced it might become widespread

The epidemiology of autumn encephalitis in Siberia the virus of which is identical with that of Japanese B fever has not been well worked out to date

Transmission of equine encephalomyelitis by mosquitoes has been proven experimentally on numerous occasions Kelser (19) in 1933 showed that *Aedes aegypti* could transmit the virus from guinea pig to guinea pig and from guinea pig to horse Since that time other mosquitoes have been implicated Some mosquitoes especially *Culex pipiens* and *Anopheles maculipennis freeborni* become infected in nature but lose all trace of the virus in 24 hours They are not of epidemiologic importance therefore It would seem that mosquitoes become infective when feeding upon a host that has been infected (experimentally) 48 to 72 hours previously that they sometimes fail to become infective when the host is inoculated 96 to 120 hours previously and never so when 144 hours have elapsed before the mosquitoes feed on the host (19) Infected mosquitoes are capable of transmitting the virus to a new host within six days after ingesting the virus and as late as 18 days

The wood tick (*Dermacentor andersoni*) and the dog tick (*Dermacentor variabilis*) both are capable of becoming infected and transmitting the western type to susceptible animals Infected ticks carry the virus through several generations the females transmitting the virus to the egg (20)



Army M dic l M m

Fig 44—Chicken mite *Dermanyssus gallinae* probably the chief vector of the virus of equine encephalomyelitis in poultry

The assassin bug (*Triatoma sanguisuga*) was found infected under natural conditions with the western equine virus in a pasture in Kansas in which two horses had died of the disease the year previously (21)

The chicken mite (*Dermanyssus gallinae*) showed

infection under natural conditions on farms in Texas with both the western strain and St Louis strain of virus (18 22) This mite is probably responsible for perpetuating the disease in the domestic hen

The tick *Ixodes ricinus* is the responsible vector for louping ill in England Only the female ticks transmit the disease The larval ticks become infected when feeding on diseased sheep and in the following nymph stage are capable of infecting new hosts Similarly when nymphs become infected the adults are capable of transmitting the infection (23)

The tick *Ixodes persulcatus* is the vector of spring summer encephalitis in European Russia It has been demonstrated that the virus is transmitted through the egg to new generations of larvae The virus propagates in the tick without apparently doing it any harm (12)

ANIMAL RESERVOIRS

Birds are the chief reservoirs of the mosquito borne encephalitides The eastern type of virus has caused epizootics in certain birds but other types cause no clinical evidence of the infection

The domestic hen varies in resistance according to age Old hens seem to be resistant but young chickens are easily infected A large percentage of hens show antibodies and probably act as reservoirs of the virus In the Yakima Valley in Washington Hammon and his associates (24) found 30 to 50 per cent of chickens (under one year of age) infected with the western virus (table 28) Fowls from non epidemic areas give negative reactions Other domestic birds that have been found naturally infected include the duck goose and turkey

Among the wild birds which have been found naturally infected in nature are the western robin pigeon ring necked pheasant quail and prairie chicken Experimental infection has been accomplished with English sparrows gambel sparrows juncos thrashers hawks blackbirds ground owls mallard ducks storks and vultures Young birds are more susceptible than old birds

Horses and mules are susceptible to encephalomyelitis virus but they do not seem to be the natural reservoir of infection Equine encephalomyelitis is the most important horse disease in the United States at the present time Horses and mules manifest variations in clinical symptoms due probably to natural resistance and the

type of virus encountered The eastern type is the most dangerous In the Massachusetts epidemic in 1938 the attack rate was 3 5 per cent with a mortality of 90 per cent The western type has afflicted many thousands of horses The mortality is much lower than the eastern type usually around 25 per cent The St Louis virus produces antibodies in horses under natural conditions in about the same proportion as does the western virus No clinical symptoms have been observed in horses due to spontaneous infection but the typical disease can be produced by inoculation The Venezuelan type is very mild with a low death rate It has a high infectivity rate however

Other domestic animals that are possible reservoirs of infection in the United States are the cow pig sheep goat and dog The cat is immune Among the wild animals that are infected are the deer jack rabbit cottontail rabbit pocket gopher brown rat black rat and probably others (25) Infection by intracranial inoculation is possible with the mouse guinea pig white rat hamster chipmunk young groundhog Richardson squirrel cotton squirrel kangaroo rat wood rat certain wild rabbits and various species of wild mice Hammon found in endemic areas that animals over one year of age gave positive serologic reactions for the St Louis type in a much larger percentage of cases than those under one year of age The same was true for western equine virus (table 28) Another

Table 28 —PERCENTAGE OF POSITIVE SEROLOGIC REACTIONS AMONG DOMESTIC AND WILD ANIMALS AND BIRDS BY AGE GROUPS (HAMMON 25)

	UNDER ONE YEAR		OVER ONE YEAR	
	Mammals	Birds	Mammals	Birds
St Louis viru	18%	35%	44%	54%
Western equine virus	2 %	39%	4? %	55%

interesting observation was the fact that in the domestic group of animals 36 per cent gave positive reactions while only 8 per cent of the wild animals reacted

Japanese B encephalitis transmitted by the mosquito is found in various birds rodents and dogs The Russian autumn virus has been isolated from the blood of birds also Horses in endemic areas show antibodies in 35 per cent of animals tested (7)

Louping ill is primarily a disease of sheep Cattle may contract the disease when grazed on infected areas but the disease is apparently of less importance in them Hogs and horses are susceptible

by artificial inoculation but conclusive evidence is lacking that they often contract the disease naturally Laboratory animals may be infected artificially either by instilling the virus into the nose or by intracerebral injection Monkeys (26) and mice (27) especially are susceptible by the intranasal route Rats show no symptoms when infected by this method although the virus may be demonstrated in the olfactory bulbs and antibodies appear in the serum (28)

Wild rodents such as squirrels and hares are the principal reservoirs of Russian spring summer encephalitis

EQUINE ENCEPHALOMYELITIS IN HORSES

In the United States the disease occurs during the summer and early fall affecting horses and mules of all ages After an incubation period of one to three weeks infected animals show a lassitude and lack of spirit accompanied by slight incoordination and peculiar gait More severe cases stagger and fall struggling in vain to get up In the advanced stages the animals are quiet They show an inability to swallow much grinding of the teeth and fibrillar spasms of the muscles of the face and limbs Severe cases die in three to eight days Milder cases may exhibit a drowsiness, the animal leaning against a tree or other support with drooping head yawning occasional grinding of the teeth and a peculiar twisting of the lips to one side Other mild cases may walk and circle continuously (29) Mild and atypical cases probably escape recognition

Recovery from the disease is not always accompanied by immunity Meyer found a few animals capable of reinfection Records and Vawter (30) in 1934 developed a method of actively immunizing horses which will carry the animals over a period longer than the prevalence of the disease during any one season in a given locality

LOUPING ILL IN SHEEP

Louping ill in sheep is characterized by a cerebrellar ataxia and disorder of the brain and spinal cord functions The incubation period is six to eighteen days in naturally infected flocks The duration of illness varies from about one day in acute infections to several weeks in chronic cases Abortive attacks are common where the only symptom may be dullness accompanied by a febrile reaction Demonstration of the virus in the blood serves to diagnose the disease

Mortality of definitely clinical cases is high Chronic cases usually show a paralysis of one or more limbs for some weeks Recovered cases are apparently immune

The tick *Ixodes ricinus* is found in hilly grazing country and when sheep are turned into infested pastures they contract the disease Not all pastures in the tick region seem to be infested with ticks however Whether tick eradication as a measure of controlling the disease is economically feasible is a doubtful question

THE DISEASE IN MAN

All types of the arthropod borne encephalitis virus cause similar clinical symptoms in man varying only in severity and mortality The onset is sudden with fever chills headache nausea and pain in the neck, back and other portions of the body Young children may show convulsions Drowsiness develops and in some cases progresses to coma Recovery begins after ten to fourteen days

The St Louis type and Japanese B type are more apt to attack the older age groups 82 per cent of cases being found in persons over 50 years of age in the St Louis outbreak The distribution between males and females is about equal Among those who survive nervous and mental sequelae are rare (table 29)

Table 29 —THE ARTHROPOD BORNE ENCEPHALITIDES

DISEASE	USUAL HOST	USUAL VECTOR	INFECTION IN MAN
St Louis Encephalitis	Birds various animals	Mosquitoes	Adults mostly Mortality 35%
Japanese B Encephalitis	Birds rodents	Mosquitoes	Adults mostly Mortality 60%
Russian Autumn Fever	Birds horses	Mosquitoes	High mortality rate
Western Encephalomyelitis	Birds horses and other animals	Mosquitoes	Adults mostly Mortality 10%
Eastern Encephalomyelitis	Birds horses and other animals	Mosquitoes	Children mostly Mortality 75%
Venezuelan Encephalomyelitis	Birds horses and other animals	Mosquitoes	Mild infection in man
Louping Ill	Sheep	Ticks	Rare in man No mortality
Russian Spring-Summer Encephalitis	Rodents	Ticks	Adults mostly Mortality 30%

The western type is found more often in adult males The disease is milder with a fatality rate of about 10 per cent This type has caused the largest number of cases in man In 1941 there were more than 3000 cases in the United States and Canada North Dakota showed the highest rate with 1080 cases and 96 deaths

In the Yakima Valley in Washington Hammon (5) showed that the presence of antibodies for the St Louis virus and western virus in the blood of the inhabitants depended on the length of residence in the Valley Persons who had resided there three years or less showed 9 1 positive while inhabitants of 12 to 20 years were 76 9 per cent positive

The eastern virus is far more dangerous The disease shows a predilection for children with a death rate of 75 per cent If the child survives paralysis and mental changes may follow The total number of cases in man has not been large In the Massachusetts outbreak in 1938 34 cases were reported The virus has been spreading however with a scattering of reports from numerous communities

The Venezuelan virus produces an illness much milder than the eastern western or St Louis types In Venezuela it does not form a public health problem of much importance The virus seems to be highly infective however because laboratory workers have been the victims on several occasions (31) In 1943 there was an explosive outbreak on the island of Trinidad at which time two human deaths occurred the first deaths attributed to the Venezuelan type

Louping ill virus causes few human infections In England there have been no cases reported among sheep herders or others connected with sheep where the disease is endemic There have been several laboratory infections however among persons working with the English strain of the virus including three in the United States in 1933 (32) one in England and one in Germany (33) Another American case occurred in 1942 There were no deaths among these cases

Russian spring summer disease appears in localized epidemics confined for the most part to solitary hamlets situated in valleys covered with thick forests The majority of cases occur in actual forest workers hence the term forest spring encephalitis used by the Russians Adult men are the chief sufferers with almost no cases in aged persons or children The fatality rate is about 30 per cent

Neutralization tests made by Rivers (32) with the blood serum of 63 persons in New York indicated that most persons suffering from miscellaneous diseases showed no protection against the English strain of louping ill virus Among seven persons who had been in close contact with the virus in the course of their laboratory duties five exhibited neutralizing substances Four of these were recovered cases of louping ill while the fifth was a laboratory worker who had had no visible signs of illness It has been suggested that repeated subinfectious doses of the causative agent might account for gradual acquired immunity among regional populations such as the sheep herders in England (34)

Casals and Webster (12) found positive complement fixation and neutralization tests with the Russian encephalitis virus in the serum of a patient who had recovered from a laboratory infection of louping ill Another patient who had been infected with either the English or Russian virus gave positive reactions against both

PREVENTION AND CONTROL

The prevention of arthropod borne encephalitides infection consists in the control of the arthropod vectors Early recognition of the disease in man is important Patients must be protected against mosquitoes and anti mosquito measures instituted The task is a difficult one however Vaccination has been attempted but not too successfully Heath found that two doses of vaccine produced antibodies in only half of the people so treated (30) The Russians have used a formalized tissue vaccine to protect man against the spring summer type of disease Laboratory workers veterinarians and others who are associated with the disease in animals or handle the virus must observe special care

Immunization of horses and mules with chick tissue vaccine prevents equine encephalomyelitis In the United States Army no cases of the disease in animals have occurred since the adoption of the immunization program A bivalent type of vaccine is administered annually in two doses of 2 c c each Other methods of control in the face of epidemics include the quarantine of animals during the summer in known areas of infection to prevent shipment to uninfected areas the eradication of mosquitoes ticks and chicken mites and the control of birds as far as possible which may act as reservoirs of infection

Tick control measures seem to be indicated for the prevention

of louping ill in sheep and Russian spring summer fever in man.

Infection by contact usually does not occur Experimental evidence seems to corroborate this view Healthy guinea pigs remain free of the disease when placed in the same pens with infected guinea pigs Likewise healthy horses have been placed with infected horses eating and drinking in intimate contact with no cross infection (14) Infection through abrasions is a possible but probably not a usual mode Infection of man by inhalation is a possibility especially through dried tick feces

ITEMS OF NOTE

1 The arthropod borne encephalitides form a group of rather closely related diseases
2 They are all caused by filtrable virus
3 Mosquitoes are the principal vectors of the St Louis type the western equine type the eastern equine type, the Venezuelan type the Japanese B type and the Russian autumn type
4 Ticks are responsible for the spread of louping ill and the Russian spring summer type
5 Birds are the chief host of the disease in the United States Japan and Siberia Horses, rodents and other animals are secondary hosts
6 Sheep seem to be the chief host of louping ill in England
7 All types of virus cause similar symptoms in man the chief difference being in severity
8 Prevention consists largely in the control of mosquitoes and ticks Horses are successfully immunized while the Russians have perfected a vaccine for man against the spring summer type of disease

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CHAPTER XV

RIFT VALLEY FEVER

Rift Valley fever is primarily a disease of sheep and cattle secondarily man is infected through contact with diseased animals The term enzootic hepatitis has also been used

HISTORY

Rift Valley fever has probably existed for many years in British East Africa In 1912 there was an epidemic of unknown etiology that carried off numbers of newborn lambs at the Government Farm and surrounding farms in the Rift Valley Montgomery in 1913 in his *annual report of the Kenya Colony* recorded what is probably the first description of the disease There is little that can be found about the infection in the years that followed although there were probably some cases that occurred (1)

In 1930 another severe epidemic occurred in the same locality as the first destroying 3 600 ewes and 1 200 newborn lambs in seven weeks Daubney Hudson and Garnham (2) made a careful study of the outbreak isolating a filterable virus as the causative agent

PREVALENCE AND DISTRIBUTION

Rift Valley fever has occurred principally in the Rift Valley of the Kenya Colony There is some evidence to believe that it exists also in the Naivasha district as well as in the French Sudan

During times of epidemics in sheep the disease may prevail to a considerable extent among persons who have any contact with the animals During the first five years 1930 34 that the disease was known as an entity about two hundred human cases were reported in the Rift Valley

THE ETIOLOGIC AGENT

The causative agent of Rift Valley fever is a filterable virus first described by Daubney (2) and his coworkers in 1931 and later con

firmed by Findlay (3) The size of the virus particles are between 23 and 25 uu Mackenzie (4) cultivated the virus through 13 consecutive transfers in a medium of chick embryo and Tyrodes solution without loss of titer

INSECT VECTORS

Mosquitoes are believed to be responsible to some extent for transfer of the virus from animal to animal Daubney and Hudson (7) showed that certain species of *Mansonia* mosquitoes carried the virus for nine days after feeding on infected blood Further evidence is added to the mosquito theory by the fact that animals protected from mosquitoes by screens did not contract the disease under natural conditions In practice one method of dealing with an epidemic has been to move sheep to higher altitudes away from mosquito territory

There may be other arthropod vectors The tick *Rhipicephalus appendiculatus* in its nymphal stage is infective for seven days after feeding on an infected sheep After moulting the tick is no longer infective (8)

THE DISEASE IN ANIMALS

The disease in animals runs an extremely rapid course The only observable symptoms may be a listlessness lack of desire for food and progressive weakness Within twenty four hours from the time the first symptoms are noticed the animals may be dead

Young lambs have a mortality of 90 to 95 per cent ewes show a mortality of 50 per cent Cattle are susceptible but have a relatively low mortality as do goats Cats may be infected as well as certain kinds of monkeys—especially Indian and South American but not African monkeys Rats and mice may be infected and are quite susceptible Daubney and Hudson found the East African rodents so highly susceptible that it is believed they play a part in the dissemination of the disease

THE DISEASE IN MAN

Man seems to be very susceptible to Rift Valley fever During the 1930 epidemic in Kenya every native herder engaged with sick sheep became infected Four Europeans who were studying the etiology of the disease likewise all developed the disease Daubney carried some of the virus to England for further study but both the

investigator and his two assistants were soon infected (5) Virus sent to the United States for study resulted in a fatal infection for the laboratory investigator (6)

The incubation period is five to six days In a native volunteer who was inoculated it was only three days The disease in man runs a rather mild course ordinarily with a temperature of 102°F to 104°F with general malaise pains in the joints and sometimes nausea After three or four days the symptoms subside Blood of patients has been demonstrated to be infective for sheep for six days after symptoms appear The virus is not found in the urine

Immunity after infection is present for at least three years Immune serum from such recovered cases has been tried for treatment purposes but with not too much success

The complement fixation reaction is of some assistance in diagnosis

ITEMS OF NOTE

1 Rift Valley fever is primarily a disease of sheep and cattle
2 It is caused by a filtrable virus
3 The disease has probably existed many years but it received little attention prior to 1930
4 There is no record of infections occurring outside of Africa except in laboratories
5 Man is exceedingly susceptible when exposed to infection

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CHAPTER XVI

MILK SICKNESS

MILK sickness in man and trembles in animals results from poisoning with the white snake root or the rayless goldenrod The disease is primarily one of animals transmitted to man through the milk or milk products of affected cattle Other names by which milk sickness has been known are white snake root poisoning slows and puking fever in the East and milk sick or alkali disease in the West

HISTORY

Milk sickness was recognized as early as 1776 in North Carolina It was a serious affliction of the early settlements of the Middle West taking many lives in Tennessee Ohio Indiana Illinois Missouri and other Mississippi River states

Mather in the Making of Illinois mentions it in connection with the settling of the New Design in 1797 stating that it attacked many newcomers It was one of the diseases which gave Illinois the reputation of being unhealthful and so retarded immigration to this territory for awhile

Herndon in his life of Abraham Lincoln describes the ravages of milk sickness in Kentucky telling how whole settlements were abandoned to get rid of the peculiar malady In the fall of 1818 the scantily settled region in the vicinity of Pigeon Creek—where the Lincolns were then living—suffered a visitation of that dread disease common in the West in early days and known in the vernacular of the frontier as the milksick! It hovered like a spectre over the Pigeon Creek settlement for over ten years and its fatal visitations and inroads among the Lincolns Hanks and Sparrows finally drove that contingent into Illinois It not only took off the people but it made sad havoc among the cattle One man testifies that he lost four milk cows and eleven calves in one week This in

addition to the risk of losing his own life was enough he declared to ruin him and prompted him to leave for points farther west! Early in October of the year 1818 Thomas and Betsy Sparrow fell ill of the disease and died within a few days of each other Thomas Lincoln performed the services of undertaker Meanwhile Abe s mother had fallen a victim of the insidious disease Her sufferings however were destined to be of brief duration Within a week she too rested from her labors

At the fifth annual meeting of the American Medical Association in 1852 Daniel Drake was appointed chairman of a Committee on Milk Sickness So Called In his report to the Association in 1858 he elaborated very extensively the theory that eating the *Rhus toxicodendron* produced the disease in cattle (8) In 1861 evidence was produced which tended to confirm the relation of white snake root to the disease in cattle In 1907 Brown (1) called attention to the sweetish odor of the breath and Walsh (2) diagnosed the human disease as an acidosis

Alkali disease had been known in the Pecos Valley of New Mexico and Texas since its earliest settlement

The poisonous properties of the rayless goldenrod were first brought to the attention of the United States Department of Agriculture when E O Wooten (3) of Mesilla Park New Mexico submitted a specimen of the plant together with a history of losses in horses and cattle Since that time a considerable number of reports have been recorded of alkali disease and milk sickness in New Mexico and Texas The exact nature of the poison responsible for the disease was unknown In 1909 Moseley (4) published a report in which he ascribed the cause to aluminum salts in the plant The work of Jordan and Harris (5) indicated that it was of bacterial nature—*Bacillus lactimorbi*—but these findings were not confirmed by other investigators

In 1926 Couch (6) of the United States Department of Agriculture isolated from white snake root and the rayless goldenrod the chemical substance responsible for the trouble It has been named tremetol

THE POISONOUS PLANTS

Two plants are responsible for milk sickness white snake root and the rayless goldenrod

White snake root (*Eupatorium ageratoides or urticaefolium*)

also called richweed boneset polewort or squaw weed grows from Minnesota to Louisiana and east to North Carolina There are over forty species of white snake root in the United States but this is the only one that has given serious trouble One other member *Fupatorium serotinum* has been suspected of causing death in animals but evidence has not been confirmed The common thoroughwort belongs to the same family and grows in the same locality

Eupatorium ageratoides grows in densely wooded areas When the trees and underbrush are removed sufficiently to permit the growth of bluegrass the white snake root disappears almost completely The plants do not thrive in the bright sunlight It has been known to grow in pastures however and is found sparingly over a wide area in urban and rural communities

In the more highly cultivated agricultural sections it has been found in orchard pastures

The plant is a slender erect perennial herb which grows from one to four feet high The leaves are opposite each other three to five inches long broadly ovate with sharply toothed or serrated edges The leaf stalks are about one fourth to one half as long as the leaf Each leaf has three main veins which extend from the base of the leaf and which give off many branches In the late summer the white flowers of the plant appear as compound clusters having eight to thirty flowers giving to pastures in heavily infested woodlands an attractive appearance Other members of the family including *Eupatorium serotinum* grow more abundantly in open pastures

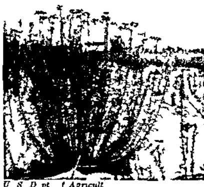


FIG 45—Rayless Goldenrod

The rayless goldenrod or jimmy weed (*Aplopappus heterophyllus*) is distributed over a wide territory from southern Colorado to the Texas Panhandle and south to Arizona Sonora and Chihuahua It is especially abundant in the irrigated portions of the Pecos Valley in Texas and New Mexico

Aplopappus frutsiosus causes poisoning in some instances but it is less widely distributed

The rayless goldenrod belongs to the composite family bearing the flowers in compact heads as does the sunflower It is a stout erect tufted perennial herb of one or two feet in height except on the banks of irrigated ditches where it grows four feet or more high The leaves are alternate line like or broader, one eighth to one fourth inch wide and three fourths to two and one half inches long *The heads are numerous with or without stems in terminal* flat topped bunches each head having seven to fifteen tubular flowers

TREMETOL

Tremetol is the name given by James F Couch of the Bureau of Animal Industry of the United States Department of Agriculture to the poisonous principle found in white snake root responsible for *trembles in cattle and milk sickness in man*

White snake root contains three poisonous substances a complex alcohol a resinous acid, and a volatile oil The latter two are only slightly poisonous and do not produce trembles The complex alcohol is the substance that has been named tremetol It is an optically active alcohol of the formula $C_{16}H$ O_3 and is soluble in alcohol ether chloroform benzene and other organic solvents It is insoluble in water acids or alkalis

Tremetol may be altered by heat or by chemical reagents and when so changed it loses its poisonous properties The temperature required for the pasteurization of milk however does not affect it

Couch devised a test for tremetol in plants, in milk butter cheese or meat He described it as follows

"The suspected material is extracted with petroleum ether Ordinary gasoline may be used if it does not give a red color with sulphuric acid The solution is poured on the surface of 2 c c of concentrated sulphuric acid in a dry test tube when if tremetol is present a red color appears at the junction of the two layers Upon shaking the tube the petroleum ether layer is colored a transient red and on allowing the layers to separate the lower layer of acid is colored a fine cherry red while the upper layer is colorless If the solution is very dilute only an orange color will result"

Milk or butter that respond to the color reaction are dangerous to health and should not be used as food A few substances other than tremetol give a red color with sulphuric acid but they are not likely to be present *when tremetol is suspected*

Tremetol is rapidly destroyed by drying so that completely dried snake root is incapable of producing trembles The poison of the rayless goldenrod on the other hand is not destroyed by drying and this plant is dangerous to cattle either green or dry

THE DISEASE IN ANIMALS

Trembles appears in pastured animals—horses cattle and sheep being the ones naturally affected During the autumn when pastures are dry white snake root is green and cattle often turn to it as a last resort Sometimes cattle will eat it even though pasture grass is abundant The course of the disease is practically the same whether due to white snake root or the rayless goldenrod

The first symptoms in cattle are drooping of head and ears dull appearance loss in weight abnormal thirst obstinate constipation and general inactivity A characteristic trembling of the voluntary muscles is responsible for the name trembles

Marked muscular debility is noted in advanced stages when the animal lies prostrate on the ground unable to rise The breath has a marked pungent odor The pulse and respiration become irregular and slow as coma appears followed by death Not all cattle in a herd develop the disease while the severity of symptoms of those infected varies in different animals

Milk cows exposed to white snake root may transmit the poison through the milk without showing any symptoms of the disease It would appear that the milk absorbs the poison thus protecting the animal in lactation When the animal goes dry the system at once becomes susceptible and the disease runs its usual course described above Sometimes animals in lactation show symptoms however

The disease runs a more rapid course in horses than in cattle The usual symptoms seen in cattle are observed Paralysis of the throat results in slobbering which is an early symptom Death follows in two or three days

Sheep exhibit symptoms similar to those seen in cattle A drowsy sleepy condition bordering on coma usually precedes death

No animal probably is immune from trembles for in addition to horses cattle and sheep it has been observed in mules swine chickens rabbits dogs cats and guinea pigs (9)

Prevention of trembles is better than attempts at cure Each case that arises may be treated separately under the care of a veterinarian but cure is not always certain

THE DISEASE IN MAN

Milk sickness in man is the result of ingesting the poison tremetol from milk butter or cheese from cattle which have partaken of white snake root or the rayless goldenrod The poison is cumulative causing a restless weak exhausted languid feeling during the early stages of the disease Later abdominal pains develop with nausea vomiting constipation thirst loss of appetite weak pulse labored breathing and subnormal temperature The throat and intestinal tract apparently become paralyzed and in fatal cases death is often preceded by a prolonged coma The incubation period is two to twelve days Acetone breath is a characteristic symptom The fatigue may last a long time with characteristic recurrences Walsh describes a case poisoned in 1924 and repoisoned again in August 1925 Three months after the poisoning strenuous exercise brought on a marked attack of the disease Relapses are common and the mortality is high in such instances

Milk sick patients often find difficulty in retaining solid food and for this reason are put on a milk diet If the milk was taken from the same source as the milk which caused the sickness in the first place the condition of the patient is rendered much worse In milk sickness an immediate change of milk and butter is imperative

Meat from animals suffering from trembles probably does not contain tremetol When dogs and cats were fed experimentally upon such meat they developed no symptoms

Couch believes that poisoned animals or man suffer from a ketosis which is a subsequent symptom to the toxic factor responsible for the onset of the disease Acetone has been demonstrated both in the urine and expired air of the lungs

The mortality from milk sickness is about 25 per cent Wolff (10) collected records of 320 cases of which 77 died

The prevalence of the disease in man is difficult to estimate as very few of the actual cases are reported In Illinois during one summer there were newspaper accounts of fifteen deaths but death certificates were turned in by physicians for only seven cases during the year There probably occur under normal conditions not more than fifty cases of milk sickness in Illinois each year Conditions in other states where white snake root exists to any degree are not dissimilar Education of the public has had a marked effect upon human affections

PREVENTION

The prevention of trembles in cattle depends upon avoiding pastures badly infested with white snake root Cattle horses and sheep should be kept out from July 1 to December 1 or until the pastures are cleaned of the weed This may be accomplished by systematic pulling of the plants in August and September while the flowers are in bloom and repeated in October After the plants have been pulled and allowed to dry they should be burned to destroy the seed Prevention of milk sickness in man depends upon avoiding milk products from affected cattle

Milk intended for human consumption is not rendered safe by pasteurization Under ordinary market conditions however such poisoned milk is diluted sufficiently with milk from other sources to render it harmless There need be no fear among city dwellers of outbreaks of milk sickness of great magnitude Milk sickness is a rural problem and education therefore must be with the farmer

ITEMS OF NOTE

1 Milk sickness is due to a chemical poison found in the white snake root plant or the rayless goldenrod This is in distinction to the other animal diseases which are bacterial in nature
2 Tremetol a complex alcohol is the responsible agent in white snake root The toxic agent in the rayless goldenrod is somewhat different in nature
3 The poison is of danger chiefly to cattle horses and sheep
4 Man is poisoned from ingesting milk or milk products from affected cattle
5 Tremetol in milk is not destroyed by pasteurization temperatures
6 Market milk is ordinarily rendered safe by dilution of the poisoned milk with milk from other sources
7 Milk sickness in man is largely a rural problem

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THE DISEASE IN MAN

Milk sickness in man is the result of ingesting the poison tremetol from milk butter or cheese from cattle which have partaken of white snake root or the rayless goldenrod The poison is cumulative causing a restless weak exhausted languid feeling during the early stages of the disease Later abdominal pains develop with nausea vomiting constipation thirst loss of appetite weak pulse labored breathing and subnormal temperature The throat and intestinal tract apparently become paralyzed and in fatal cases death is often preceded by a prolonged coma The incubation period is two to twelve days Acetone breath is a characteristic symptom The fatigue may last a long time with characteristic recurrences Walsh describes a case poisoned in 1924 and repoisoned again in August 1925 Three months after the poisoning strenuous exercise brought on a marked attack of the disease Relapses are common and the mortality is high in such instances

Milk sick patients often find difficulty in retaining solid food and for this reason are put on a milk diet If the milk was taken from the same source as the milk which caused the sickness in the first place the condition of the patient is rendered much worse In milk sickness an immediate change of milk and butter is imperative

Meat from animals suffering from trembles probably does not contain tremetol When dogs and cats were fed experimentally upon such meat they developed no symptoms

Couch believes that poisoned animals or man suffer from a ketosis which is a subsequent symptom to the toxic factor responsible for the onset of the disease Acetone has been demonstrated both in the urine and expired air of the lungs

The mortality from milk sickness is about 25 per cent Wolff (10) collected records of 320 cases of which 77 died

The prevalence of the disease in man is difficult to estimate as very few of the actual cases are reported In Illinois during one summer there were newspaper accounts of fifteen deaths but death certificates were turned in by physicians for only seven cases during the year There probably occur under normal conditions not more than fifty cases of milk sickness in Illinois each year Conditions in other states where white snake root exists to any degree are not dissimilar Education of the public has had a marked effect upon human affections

CHAPTER XVII

INFECTIONS PRODUCED BY ANIMAL PARASITES*

DURING the centuries of man s prehistory when he was intimately associated with animals on which he depended for food and clothing he was undoubtedly exposed to more types of infectious organisms parasitizing these animals than he is today In some in stances the parasites must have produced diseases of epidemic or pandemic proportions in the human population but infected indi viduals who survived frequently developed a more or less useful resistance or immunity to the parasites In certain cases the strain of the parasite in man became physiologically distinct from that in the animal host (viz *Ascaris* of man and the pig) and in time the reservoir host ceased to be a source of infection for man Later the dependence on plant as well as animal food somewhat lessened man s exposure to certain diseases while on the other hand the domestication of animals parasitized by organisms to which man was susceptible increased the likelihood of infection in the human host Thus the relationship of reservoir hosts to human infection with animal parasites has been one of progressive change modified at least in part by changes in the habits and modes of life of groups of the human population

The methods by which man is exposed to infection with parasites commonly or incidentally infecting domesticated or wild animal hosts may be grouped for the most part into the following categories

1 Cysts eggs or larvae of the parasite are accidentally taken into the mouth in food or drinking water contaminated with feces of the reservoir host Examples Cysts of *Balantidium coli* eggs of *Hymenolepis nana* from the murine host larvae of *Trichostrongylus* from herbivorous mammals

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* Prepared by Ernest Carroll Faust Ph D Department of Tropical Medicine Tulane University New Orleans La

6 Couch J F U S Dept Agri Bur An Ind Circular Letter on Milk Sickness Oct 1926
7 University of Illinois Div of Animal Pathology Exchange Aug 1927
8 Drake Daniel Tr A M A 1858 *11*
9 Couch J F U S Dept Agri Circ 306 1933
10 Wolff F A Curtis R S and Kaup B F North Carolina Agri Exper Sta Tech Bull 15 1918

is a dangerous parasite of man in warm climates This organism burrows into the wall of the large bowel producing narrow necked but basally enlarged deeply excavated lesions comparable to those of *Endamoeba histolytica* on a somewhat larger scale Human infection is most probably acquired from contamination of food or drink with pig droppings which contain the encysted organisms Patients with balantidiasis usually give a history of close association with pigs However the relatively low incidence in man compared with the amount of exposure suggests a considerable degree of refractiveness to the infection The infection in the porcine host is apparently harmless but that in man is either acute or chronic almost never of a symptomless carrier type Furthermore there is no satisfactory drug for the eradication of the infection in the human host

Some species of hemoflagellates (i e those flagellate Protozoa which have become adapted to the blood stream the cells of the reticulo endothelial system and at times other tissues of the body of vertebrates) are common parasites of both wild or domesticated mammals and man *Leishmania donovani* the agent of visceral leishmaniasis (kala azar) and *L tropica* the agent of cutaneous leishmaniasis (Oriental sore Delhi boil Aleppo button etc) have reservoirs in the dog (China Iraq Iran Mediterranean countries) and in wild rodents (southern U S S R) and probably constitute important sources for infection of the sand fly which is the insect vector of these diseases The human trypanosomes are also related to reservoir infections in wild and domestic mammals *Trypanosoma gambiense* and *T rhodesiense* are the species of organisms causing African sleeping sickness in man Clinically and possibly biologically these organisms are specifically different from one another as well as from *T brucei* of big game animals and domestic cattle Morphologically however these three species are apparently identical and are transmissible to the next mammalian host by the same species of tsetse flies Nevertheless *T gambiense* and *T rhodesiense* have become so specifically adapted to the human host that they are not readily infective for cattle or game animals and similarly *T brucei* is apparently not adapted for residence in man A much closer association is found in *Trypanosoma cruzi* which has an extensive distribution from Central Chile and Northern Argentina to the Southwestern United States although human infection has not been reported north of Southern Mexico This parasite utilizes various species of assassin bugs as intermediate hosts and transmitting

2 The larval stage of the parasite actively enters the human body from the soil or water Examples *Ancylostoma braziliense Schistosoma japonicum*
3 The larval stage of the parasite in the tissues of an intermediate host is accidentally or unknowingly swallowed Examples Cysts of *Trichinella spiralis, Clonorchis sinensis*, etc larvae of *Taenia saginata* or *Diphyllobothrium latum* larvae of *Dracunculus medinensis* and *Dipylidium caninum*
4 The intermediate host introduces the organism into or onto the human skin at the time of obtaining a blood meal Examples *Trypanosoma gambiense* transmitted by tsetse flies *T cruzi* transmitted by assassin bugs
5 The parasite developed in or on the reservoir host actively invades the human body from the air or ground Example Myiasis producing flies

It must be understood that the problem of human infection with animal parasites is a serious one in so far as reservoir hosts are involved only when the parasite is a relatively common invader of both the reservoir host and man and when the strains of these parasites in the two types of hosts are physiologically adapted to invasion and infection of the reciprocal host Hundreds of species of animal parasites which commonly infect reservoir hosts are only incidental or rare parasites of man but comparatively few species commonly occur in both types of hosts Special consideration will be given only to this smaller group

PROTOZOAN PARASITES

Among the large numbers of species of Protozoa described from vertebrate hosts very few indeed are known to infect man *Endamoeba histolytica* the only ameba pathogenic for man is a natural parasite of monkeys and less frequently of dogs and cats but the opportunities for transfer of the cysts (which are the infective stage) from these beasts to man are very few when compared with the daily chances of human carriers producing contamination of food and drink

No intestinal flagellates (Class Mastigophora) or coccidia (Class Sporozoa) of domestic or wild animals are known to be infective for man

One intestinal protozoan *Balantidium coli* a ciliate species commonly found in the large bowel of monkeys and the domestic pig

is a dangerous parasite of man in warm climates This organism burrows into the wall of the large bowel producing narrow necked but basally enlarged deeply excavated lesions comparable to those of *Endamoeba histolytica* on a somewhat larger scale Human infection is most probably acquired from contamination of food or drink with pig droppings which contain the encysted organisms Patients with balantidiasis usually give a history of close association with pigs However the relatively low incidence in man compared with the amount of exposure suggests a considerable degree of refractiveness to the infection The infection in the porcine host is apparently harmless but that in man is either acute or chronic almost never of a symptomless carrier type Furthermore there is no satisfactory drug for the eradication of the infection in the human host

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agents The many reservoir hosts include armadillos opossums squirrels bats, numerous species of rodents, monkeys dogs and cats From these reservoir hosts the disease is readily picked up by the blood sucking bugs and after an incubation period inoculated into unsuspecting human beings

While there is suggestive evidence that the malaria parasites of man are closely related to and may have been derived from the plasmodia in other primate hosts there is no conclusive morphological or experimental proof that human malaria is today caused by organisms originating in non human sources

Some parasitologists regard toxoplasmosis, produced by one or more species of *Toxoplasma* as a protozoan infection Species of this organism not uncommonly parasitize certain rodents and birds but it is uncertain whether the organism which produces disease in man is identical or specifically different Another organism of uncertain relationship is *Sarcocystis* which is possibly akin to the Protozoa of the class Sporozoa (Sarcosporidia) but has more recently been shown to have characteristics which would place it among the fungi On rare occasions this infection has been reported from man usually at autopsy The infection involves muscle tissue and is not uncommon in cattle sheep horses hogs rabbits mice and other mammals and related infections occur in birds and lizards While the epidemiology of sarcocystiasis is not entirely clear experimental evidence suggests that infection is acquired from food or drink contaminated with feces containing spores of the parasite

HELMINTHIC PARASITES

The Helminths or parasitic worms belong to two large groups of the Animal Kingdom the roundworms and the flatworms The roundworms (Nematoda) are the most common parasites of vertebrates Some species of roundworms parasitize invertebrates others invade healthy plant tissues and by far the largest number of species is free living Forms of human importance include *Trichinella spiralis* the hookworms and their allies *Strongyloides stercoralis Ascaris lumbricoides Trichocephalus trichiurus* the filarial worms and *Dracunculus medinensis* The flatworms consist of two parasitic groups *the tapeworms and the flukes and in addition* two non parasitic groups the turbellarians and the nemerteans Common tapeworms of man include the beef and pork tapeworms the broad (fish) tapeworm and the dwarf tapeworm Many of the human

flukes are clinically very important in certain portions of the world where the appropriate intermediate hosts occur and the habits of the human population are such as to expose them to infection

THE TRICHINA WORM *TRICHINELLA SPIRALIS*

This nematode which has a cosmopolitan distribution is most common as a human parasite under conditions where raw or inadequately cooked pork is consumed by man The worm was first discovered by Peacock at a human autopsy in London in 1828 and was first obtained from hog s flesh by Joseph Leidy of Philadelphia in 1846 Leuckart (1855) and Virchow (1859) first demonstrated the life cycle and Zenker (1860) the clinical importance of the infection Except in the Balkan states the disease is much less important in Europe than it was a century ago but in the United States

Table 30 —INCIDENCE OF TRICHINOSIS AND CONDITION OF TRICHINAE BY AGE AT DEATH IN 855 POSITIVE CASES (WRIGHT JACOBS AND WALTON 1944)

AGE AT DEATH	TOTAL NUMBER CASES	POSITIVE CASES		CONDITION OF LARVAE		
		Number	Percent	Live	Mixed	Dead
1-44	1 967	248	12 6	102	65	81
45 and over	3 304	603	18 3	143	77	383
1-4	85	1	1 2	1	—	—
5-9	63	4	6 3	—	1	3
10-14	65	8	12 3	4	3	1
15-19	123	7	5 7	4	2	1
20-24	195	21	10 8	10	7	4
25-29	228	27	11 8	14	8	5
30-34	251	37	14 7	19	8	10
35-44	958	143	14 9	50	36	57
45-54	1 050	190	18 1	68	35	87
55-64	1 031	186	18 0	40	22	124
65-74	817	156	19 1	7	18	111
75 and over	406	71	17 5	8	2	61
Unknown	42	4	9 5	—	—	4
Total	5 313	855	16 1	245	142	468

(especially in New York Massachusetts Connecticut Minnesota Missouri and California) a marked increase in incidence of the infection in man has been reported within the last decade This may be due to a more careful laboratory and postmortem diagnosis or to an actual increase in cases

Infected hog meat contains the encysted *Trichinella* larvae When this meat is eaten raw or inadequately processed the larvae are digested out of the flesh in the patient s stomach become excysted in the duodenum and invade the duodenal and jejunal mucosa

agents The many reservoir hosts include armadillos opossums squirrels, bats, numerous species of rodents monkeys, dogs and cats From these reservoir hosts the disease is readily picked up by the blood sucking bugs and after an incubation period inoculated into unsuspecting human beings

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Table 32—SUMMARY OF 4,6[illegible]3 EXAMINATIONS MADE FOR TRICHINAE IN MAN

YEAR	AUTHOR	LOCALITY	METHOD	NUMBER OF EXAMS	INFECTED	
					Number	Per Cent
1901	Williams	Buffalo N Y	Pressed Muscle	505	26	5 3
1910	Simonds Indianapolis	St Louis	Pressed Muscle	100	[illegible]	[illegible]
1931	Queen	Rochester N Y Boston	Digestion	402	75	18 6
1934	Riley and Scheifley	Minneapolis	Pressed Muscle	117	20	17 1
1936	Hinman New Orleans	New Orleans	Digestion	200	7	3 5
1936	McNaught and Anderson	San Francisco	Digestion	200	48	24
1937	Hall and Collins	Washington D C	Digestion and Pressed Muscle	300	41	13 6
1937	Queen	Denver Colo	Digestion	431	70	16 3
1937	Magath	Rochester Minn	Pressed Muscle	220	17	8
1937	Scheifley	Minneapolis and St Paul	Pressed Muscle	118	15	12 7
1938	Walker and Breckenridge	Alabama	Digestion and Compression	100	33	33 0
1939	Sawitz	New Orleans La	Digestion	400	24	6 0
1939	Butt and Lapeyre	Los Angeles Cal	Digestion	170	31	18 2
1939	Harrell and Johnston	Durham N C	Digestion and Compression	10	3	2 8
1940	Oosting	Dayton O	Digestion	134	27	20 1
1940	Cator	Ann Arbor Mich	Digestion	300	44	14 7
1940	Gould	Detroit Mich	Digestion and Compression	500	93	18 6
1941	Merrill	Northern Utah		47	0	0
1941	Meleney	Nashville Tenn	Digestion and Compression	209	21	10 0
1944	Br[illegible]ler and Porter	Richmond Va	Digestion and Compression	100	6	6

skeletal muscles where they are filtered out and soon become encysted Larviposition by the female worm covers a period of about six weeks The heaviest infection occurs in muscles poor in glycogen

The pathology and symptomatology of trichinosis is divided into three periods (1) that of *invasion* of the intestinal wall with symptoms resembling acute food infection (2) that of *larval migration* with excruciating myositis and edema and (3) the *toxic* stage following encystation of the larvae with a variety of symptoms of toxic origin The disease is usually accompanied by a hypereosinophilia Although the above picture is typical of the severe cases and death or prolonged invalidism may be a sequela unquestionably an in

Table 31 —INCIDENCE OF TRICHINELLA SPIRALIS IN VARIOUS POPULATION GROUPS AS FOUND IN 5 313 POST MORTEM EXAMINATIONS (WRIGHT JACOBS AND WALTON 1944)

	TOTAL NUMBER IN GROUP	NUMBER INFECTED	PERCENT INFECTED
Males	3 736	623	16 7
White	2 757	465	16 9
Colored	915	152	16 6
North American Indians	8	1	—
Chinese	9	0	—
Japanese	4	1	—
Filipinos	10	0	—
Mexican	25	3	—
Race unknown	8	1	—
Females	1 575	232	14 7
White	942	140	14 9
Colored	608	86	14 1
North American Indians	8	0	—
Japanese	1	0	—
Mexican	10	4	—
Race unknown	6	2	—
Sex unknown	2	0	—
Whites	3 699	605	16 4
Negroes	1 523	238	15 6
Other race	75	9	—
Race unknown	16	3	—
Military (Army Navy)	324[1]	41	12 7
Officers (commissioned and warrant)	117	19	16 2
Enlisted *men*	207[1]	22	10 6
Army	203	27	13 3
Navy	121[2]	14	11 6
Families and relatives of military men	64	11	—
Civil	4 984	813	16 3
Civilian Conservation Corps	54[3]	5	—
Farmers	289	48	16 6
Villagers	147	16	10 9
Veterans mostly World War	765	157	20 5
Military Civil status unknown	5	1	—
Sea (Navy Merchant Marine)	300	36	12 0
Merchant Marine	179	22	12 3
Land	5 013	819	16 3
Mentally deranged under hospitalization	684	115	16 8
Mentally sound or not under hospitalization	4 629	740	16 0
High economic social status	1 189	179	15 1
Low economic social status	3 788	630	16 6
Economic-social status unknown	336	46	13 7
Total cases	5 313	855	16 1

[1] One case both soldier and sailor counted only once
[2] One case both soldier and sailor counted in both group
[3] Two case both CCC and veteran counted in both group

where in *three to five days they develop into adult males* (1 4–1 6 mm by 40–60 microns) and females (somewhat larger than the *males*) After fertilization the females invade the tissues of the intestinal wall more deeply and begin to deposit living young many of which burrow into the mesenteric venules and are carried to

penetrating the skin appear to be incapable of reaching the peripheral blood vessels but continue to live for weeks or months in serpiginous tunnels which they produce in the skin

Other roundworms more or less akin to the hookworms which are relatively common in domestic mammals and occasionally parasitize man include the following (1) *Haemonchus contortus* the sheep wireworm (2) *Metastrongylus elongatus* which parasitizes the respiratory tract of hogs sheep and cattle (3) *Ternidens deminutus* and species of *Oesophagostomum* which commonly infect simian hosts On the other hand *Strongyloides stercoralis* which is not uncommon in the human host and the chimpanzee in certain warm areas of the world is occasionally found in dogs which possibly obtain their infection from human sources

One of the most interesting and historically the most important roundworms is the dragon worm (*Dracunculus medinensis*) commonly found as a parasite of man in parts of India Arabia Persia and Africa Upon becoming mature the meter long female worm crawls from the patient s viscera to the skin layers and produces a little cutaneous blister at the point where its head nears the surface of the skin On contact with fresh water the blister ruptures and a swarm of active larvae is discharged These larvae may be picked up by little water fleas (*Cyclops*) in the body cavity of which the larvae mature When human beings accidentally ingest the *Cyclops* in raw drinking water they acquire the infection In China dogs are reservoirs of this worm and in the United States it parasitizes fur bearing mammals although in neither of these countries is the parasite known to infect man

INCIDENTAL ROUNDWORM INFECTIONS OF MAN

From time to time clinicians and medical parasitologists have reported cases of rare infections of man due to roundworms Almost without exception these worms are relatively common parasites of domestic or wild animals which accidentally or incidentally occur in the human subject Mention may be made of *Syngamus laryngeus* a relatively common parasite of the upper respiratory tract of cattle water buffaloes and goats with eight reported infections from man several species of *Trichostrongylus* commonly parasitizing the intestinal tract of many species of herbivorous mammals and reported on many occasions from man particularly in Asia and Africa *Gongylonema pulchrum* a relatively common esophageal parasite

creasingly larger number of subclinical cases is occurring in the United States with mild symptoms or without apparent symptoms

Diagnosis of trichinosis may be suggested by the patient s history and a high eosinophilia and is confirmed by recovery of the larvae from centrifugalized specimens of blood or from digests of biopsied samples of biceps muscle as well as by the Bachman intradermal reaction using antigen in dilution of 1 to 5 000–10 000 No specific therapeutic is known only symptomatic treatment is available

While many ideas have been advanced for the prevention of trich inosis in the human population the majority of these are imprac ticable In the United States infected pork from country slaughter houses provides the largest number of serious clinical cases but the larger government inspected slaughter houses provide little guaran tee of trichina free meat unless it has been subjected to refrigeration at 5°F for 20 days or at 2°F for 24 hours Smoking salting and drying do not necessarily kill the larvae If no garbage slops con taining infected pork trimmings or viscera were fed to hogs on the farm or in the slaughter pens the incidence and amount of infection in the hogs would soon be reduced to the vanishing point Until this protection is provided the only simple safeguard is the thorough heating of all pork to be consumed The same precaution applies to bear meat which is not infrequently infected with this parasite The rat while often harboring the parasite is of less importance than was formerly thought in spreading trichinosis to man or hogs

HOOKWORMS AND THEIR ALLIES

The two common human hookworms *Necator americanus* and *Ancylostoma duodenale* are rarely found in reservoir hosts and the common dog hookworm *Ancylostoma caninum* seldom if ever parasitizes man On the other hand, a hookworm of dogs and cats in warm climates *Ancylostoma braziliense* is a relatively important parasite of man in certain limited foci In strictly tropical environ ments as in Brazil Ceylon and the Philippines *A braziliense* is an intestinal parasite of man just as are *A duodenale* and *Necator americanus* However along the south Atlantic and the Gulf coastal areas of the United States in southern Brazil on the coast and in isolated foci elsewhere human beings exposed to the canine or feline strains of this species develop only a cutaneous manifesta tion referred to as "larva migrans or creeping eruption" This is due to the fact that the infective stage larvae of this worm on

the beef tapeworm (*Taenia saginata*) man is the only known host of the mature worm while the ox is the necessary host of the larval or *cysticercus* stage Similarly man harbors the mature pork tape worm (*T solium*) while the hog is the usual host of the larval stage The larvae (cysticerci or bladder worms) develop respec tively in the striped muscles of the ox or hog after these animals have ingested the eggs which have been evacuated in stools of in fected persons When man eats inadequately heated or inadequately processed beef or pork that is infected he acquires the infection Pork tapeworm infection is relatively uncommon in the United States but beef tapeworm infection is widely distributed in this country and elsewhere and furthermore shows no evidence of di minishing in the human population In endemic foci cattle should not be allowed to pasture on ground contaminated with polluted sewage All beef and pork should be thoroughly cooked as a simple safeguard against infection The hydatid worm (*T granulosus*) reaches maturity in the intestine of the dog and its wild relatives Eggs are discharged in dogs feces and are the source of infection in the larval stage (*hydatid cyst*) of sheep hogs cattle other herbivo rous mammals and man Control of this serious infection requires deep burying of the carcasses of sheep hogs and cattle which have died of the disease and meticulous care on the part of human beings not to allow dogs feces to contaminate food drink or mess kits

THE TREMATODES OR FLUKES

Man and the higher vertebrate animals are parasitized by only those trematodes which require some mollusc as an intermediate host (i e the digenetic trematodes) In the mollusc two or more generations of the life cycle are developed There emerge from the mollusc (usually a snail) swarms of tailed larvae called cercariae which either invade the definitive host directly *via* the skin route or first encyst in the tissues of a second intermediate host When the infected tissues of this latter host are consumed by the appro priate final host the trematode is enabled to proceed with its life cycle

The blood flukes or schistosomes produce cercariae which directly penetrate the skin of the definitive host The adults live in the portal blood stream and its adnexa and their eggs are evacuated from the host s body either in the feces or urine Of the several blood flukes living in mammals three species are relatively common in the hu

of ruminants monkeys hedgehogs, bears and pigs with at least twelve reported instances from man (buccal mucosa) *Gnathostoma spinigerum* of feline canine and other reservoir hosts and *G hispidum* of the pig producing subcutaneous abscesses and at times tunnels (so called creeping eruption) in man and *Thelazia callipaeda* the conjunctival worm of the dog as well as *T californiensis* of the dog and cat both of which have on rare occasions been recovered from the human conjunctiva

The ascaris of the hog *Ascaris lumbricoides* var *suum* is morphologically indistinguishable from that of man but is biologically different Man does not become infected from ingesting infective stage *Ascaris* eggs from porcine sources only from human sources

THE TAPEWORMS

Domestic animals play an important role in most of the tapeworm infections of man serving either as reservoir or intermediate hosts The rat and mouse are reservoirs of the dwarf tapeworm (*Hymenolepis nana*) and the rat tapeworm (*H diminuta*) while the dog and cat serve as reservoir hosts of the double pored tapeworm (*Dipylidium caninum*) *H diminuta* and *D caninum* are relatively uncommon human parasites and are acquired from accidentally swallowing infected insects which are ectoparasites of the reservoir host *H nana* requires no intermediate host It is relatively common as a human infection Although rats and mice are commonly infected with this worm they are infrequently the source of human infection since the human and rodent strains of this tapeworm are not readily infective for the reciprocal hosts Dogs serve as reservoir hosts of the broad fish tapeworm *Diphyllobothrium latum* but man is usually the indirect source of his own infection which necessarily is carried through (1) a water flea (*Diaptomus* or *Cyclops*) and (2) a fresh water fish before becoming infective for a mammalian host

Rarely man has become accidentally infected with tapeworms normally parasitic in simian hosts as for example *Bertiella studeri* or in birds as for example *Drepanidotaenia lanceolota* a common parasite of ducks

The most important relationship of domestic mammals is reservoirs or intermediate hosts of human tapeworm infections is illustrated by the species of Taenia (*T saginata* and *T solium*) and the related hydatid worm (*Echinococcus granulosus*) In the case of

ARTHROPOD PARASITES

Many insects and other arthropods prey on man and other animals A few actually invade the tissues of their victims but most of them are only ectoparasites visiting the host to obtain a blood meal

A few species of mites enter the human skin Most notorious of these is the mange mite *Sarcoptes scabiei* but it is doubtful if the variety which infests man has an animal host

The rat mite *Liponyssus bacoti* causes an itchy dermatosis affecting mainly the legs but also other parts of the body The parasite ordinarily inhabits dark crevices where it lays its eggs Hence the semi darkness of motion picture theaters and also parts of hospitals office buildings and department stores are favorable sources of infestation In cold weather the mites even turn to warmer rooms like the bathroom and kitchen They remain on the brown rat only a few hours during feeding and a lesser time on human beings It is thus only a temporary parasite of the skin like the bed bug The disease has been recognized particularly in Texas (Shelmire) since many cases are observed in Texas and Louisiana this dermatitis runs a close second to scabies in frequency of parasitic dermatoses The incidence rises during antirat campaigns when the parasite deserts its favorite host and turns to man Children are affected the more extensively with lesions on the face and hands but the ankles beltline upper parts of shoulders and neck may be involved Vesicles are present in addition to the wheals and papules observed in adults

The fowl mite *Dermanyssus gallinae* is an ubiquitous parasite that deserts sick and dead fowls whereupon the attendants of such fowls receive their attention The skin of the hands becomes scaly dry and covered diffusely by papules In severe cases pustules and crusts may form Experimental and epidemiological evidence suggests that this mite is possibly the vector of St Louis encephalitis from fowl to fowl

The chigoe (*Tunga penetrans*) and many species of fly maggots infest both man and a variety of mammalian species

THE PROBLEM OF PREVENTION OF ANIMAL PARASITES INFECTING MAN

Where man is the sole or only important host of an infection public health measures directed against the dispersal of unsterilized human excreta together with specific therapeutic procedures if

man population in endemic areas, namely *Schistosoma haematobium* (Africa and Western Asia), *S mansoni* (Africa and parts of Tropical America) and *S japonicum* (Oriental area) *S haematobium* infects man alone *S mansoni* is a parasite also of simian hosts in limited areas *S japonicum* which is distributed through extensive areas in Central and South China and occurs in a few foci in Japan Formosa and the Philippines has been recorded from dogs cats rodents cattle water buffaloes and other mammals sufficiently often to indicate the importance of these animals as reservoirs of this infection In addition *S bovis* a common parasite of domestic animals in portions of the Eastern Hemisphere has on a few occasions been diagnosed as a human infection

In contrast to the blood flukes many of those trematodes which encyst in second intermediate hosts and infect man by the buccal route are parasites common to both man and other vertebrate hosts Attention may be directed to a few typical examples From eating raw or inadequately cooked fresh water fish man and other fish eating mammals acquire infection with the Chinese liver fluke (*Clonorchis sinensis*) and its close relatives (*Opisthorchis felineus* and *O viverrini*) Canines and felines are especially prone to infection with these worms Other flukes acquired from consuming raw fish include minute heterophyoid species as *Metagonimus* and *Heterophyes* Some of these small flukes as well as species of echinostomes are more commonly parasitic in birds than they are in mammals The sheep liver fluke (*Fasciola hepatica*) is common in sheep less frequent in other mammals and man It gains entrance to the hosts body through consumption of raw vegetation on which the cercariae have encysted The giant intestinal fluke (*Fasciolopsis buski*) which is prevalent in certain areas in the Far East is a common parasite of both pigs and man in these localities The Oriental lung fluke (*Paragonimus westermani*) which mammals acquire from eating the soft parts of crabs and crayfishes parasitizes man felines and canines In the United States a closely related species *P kellicotti*, is known as a parasite of several species of fur bearing mammals but only one probable human infection is on record Potentially amphistomate flukes of the hog cattle and certain wild ruminants may infect man but reported human infections are very few Echinostomate flukes of the dog (*Echinochasmus perfoliatus*) and even of the duck (*Echinostoma revolutum*) are occasional human parasites

Creeping eruption caused by the hookworm *Ancylostoma braziliense* a parasite of dogs and cats in warm climates

Dracontiasis caused by the dragon worm *Dracunculus medinensis* a parasite of dogs in China and of fur bearing animals in the United States (although the disease does not occur in man in either of these countries)

Other roundworm infections include *Trichostrongylus* from herbivorous animals the sheep wireworm *Haemonchus contortus* from sheep and cattle *Metastrongylus elongatus* from the respiratory tracts of hogs sheep and cattle *Ternidens deminutus* from monkeys and *Syngamus laryngeus* from cattle

The thread worm *Strongyloides stercoralis* is found in dogs

Various other roundworms are occasionally acquired by man from animals

4 Tapeworm infections are rather commonly transmitted from animals to man

The dwarf tapeworm *Hymenolepsis nana* is found in rats and mice man being infected from the droppings of these rodents

The rat tapeworm *Hymenolepsis diminuta* is found in rats and mice but human infection is acquired from swallowing an infected insect

The double pored tapeworm (dog tapeworm) *Dipylidium caninum* is acquired from dogs and cats by swallowing an infected flea

The broad fish tapeworm *Diphyllobothrium latum* finds the dog as a host but man is infected by eating fish

The beef tapeworm *Taenia saginata* and the pork tapeworm *Taenia solium* are acquired from insufficiently cooked beef and pork

Hydatid disease caused by *Echinococcus granulosus* is acquired from the dog but sheep hogs cattle and other herbivorous animals are hosts

5 The trematodes—flukes—which parasitize man all require some mollusc usually a snail as an intermediate host

Several liver flukes find a host in the dog or the cat among other animals Infection with *Clonorchis sinensis* *Opisthorchis felineus* and *Heterophyes* or *Metagonimus* is contracted by these animals from eating raw fresh water fish

The sheep liver fluke *Fasciola hepatica* is common in sheep

available, should ultimately wipe out the disease But where reservoir hosts are involved, the situation is more complicated since the parasite may be propagated in spite of these control measures In such instances as well as those in which animal or plant tissue serves as the medium for transfer of the organisms to man mankind must be taught the sources of the infection and the means for protecting his food and drink as well as his skin from the invader The successful completion of this latter type of protection cannot be carried out solely by police powers of a government but requires cooperation of all individuals in the community It presupposes, therefore a higher type of civilization than is found in primitive peoples in whom diseases of animal etiology are most prevalent Yet the incidence of trichinosis and beef tapeworm infection in our supposedly civilized communities indicates that much remains to be accomplished along these lines

In the case of arthropods which serve as biological or mechanical vectors of parasitic infections there is now substantial evidence that DDT will be of inestimable aid in eradicating the vector hence the transmission of the disease

ITEMS OF NOTE

1 Numerous parasites classified in the Animal Kingdom infect or infest other animals comparatively few such parasites transmit diseases from the animal host to man
2 Protozoan parasites of animals cause the following diseases in man
   Amebic dysentery caused by *Endamoeba histolytica* a natural parasite of monkeys and sometimes of dogs and cats
   Dysentery caused by *Balantidium coli* from monkeys and domestic pigs
   Kala azar Oriental sore and allied conditions caused by *Leishmania donovani* and *L tropica* from canine and rodent hosts
   African sleeping sickness caused by *Trypanosoma gambiense* and *T rhodesiense* closely akin to trypanosomes of wild game in Africa as well as Chagas disease caused by *T cruzi* common in domestic and wild mammals in Latin America
3 Parasitic roundworms of animals are responsible for the following ailments of man
   Trichinosis caused by *Trichinella spiralis* a parasite of hogs rats and bears

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being acquired from eating raw plants which carry the encysted meta cercariae

The giant intestinal fluke *Fasciolopsis buski* is carried by the hog which acquires it from plants

The Oriental lung fluke *Paragonimus westermani* is contracted by dogs and cats from eating crabs and crayfish The closely related *P kellicotti* is found among fur bearing animals in the United States

The blood flukes *Schistosoma mansoni* of monkeys *S japonicum* of dogs cats cattle and rodents and *S bovis* of cattle penetrate the skin directly

6 Arthropods from animal hosts cause the following afflictions in man

Rat mite dermatitis by the rat mite *Liponyssus bacoti*

Poultryman s itch by the fowl mite *Dermanyssus gallinae*

7 Prevention consists in education and a better appreciation of the sources of infection In case of arthropods DDT constitutes a valuable weapon of control

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inasmuch as more than a hundred different species have been listed as pathogens (Brumpt) (4) right or wrong it is clear that in this sense the scope of actinomycosis would be wide indeed Fortunately however usage has confined the meaning to the well known clinical complex caused by *Actinomyces bovis* and for the purposes of this book the term will be used entirely in that sense Where there are possibilities of doubt the designation actinomycosis proper is in order

In the past actinomycosis and the sulphur granule have been linked inseparably but of late the pathognomonic significance of the latter structure has been melting away Studies of human tonsils in Porto Rico (Emmons) (5) indicate that culturally proven *Actinomyces bovis* occurs in the crypts simply as threads i e without the clubs which characterize the ray fungus (sulphur granule) Significantly at a subsequent examination of the same patient clubs were found It appears then that club formation is a capricious phenomenon for *Actinomyces bovis* it is probable that clubs form when the conditions for the parasite are the more adverse as in solid tissues like lungs and liver When more or less on the surface as in tonsillar crypts clubs occur but seldom Consistently with this idea it is well established that on the favorable environment of test tube cultures clubs do not form at all There is a most practical outcome of these data Whereas in the past it was sufficient to depend upon the ray fungus when evaluating actinomycosis we must now realize that there are complicating factors which may demand culture studies

Moreover club formation is not confined to *A bovis* *Actinobacillus lignieresi* and various other bacteria exhibit them Inasmuch as the clinical complexes of actinobacillosis and actinomycosis are similar pains should be taken to distinguish between these two club bearing microorganisms

Incidentally the above considerations have an important bearing on animal pathology now that *A bovis* has been found by Emmons in tonsils (47 per cent) extirpated in Porto Rico (cultures secured in 23 per cent) and because Davis found the species in the tonsils of hogs (4 7 per cent) (6) Incidentally the tonsils of cows (7) did not contain the fungus It would appear therefore that the tonsils of both hogs and man frequently contain masses of *A bovis* which living saprophytically may not produce clubs nor disease Since such granules escape readily into the mouth it can be understood

Actinomycosis in Animals

As in man actinomycosis runs a chronic course There is a predilection for the head and neck but after that any part of the body may be involved It is not very contagious Salmon kept 21 healthy cattle tied alternately between cattle infected with actinomycosis but cross infections did not occur It appears to be the consensus that as in man portals of entry are created by trifling traumatisms into which vegetable material becomes lodged

Of animals cattle are the ones most often affected The initial lesion is a granuloma resembling a tuberculoma This ulcerates and discharges thick yellowish pus It is to be emphasized however that by and large the lesions of animals are not consistently suppurative as they are in man infections around the head and neck tend to be dominantly fibrotic The tongue for example becomes hugely swollen and projects from the mouth—hence the name wooden tongue Where the mandible is attacked the lesion may be mistaken for osteosarcoma In such lesions there is osseous hyperplasia in addition to the fibrous the whole resulting in swellings perhaps the size of a football Lesions of the mammary gland are uncommon when they do occur they are often mistaken as tuberculous Patterson found 5 out of 50 cows suspected as tuberculous to be in reality infected with actinomycosis In each case the lesion was on the udder—probably infected by straw

Other animals are less commonly infected than cattle Only a few cases have concerned horses usually with involvement of the submaxillary lymph nodes In the pig lesions have been found in the mammary glands throat and castration wounds Sheep are infected on the tongue lips and in the lungs Dogs and cats have been found infected according to several workers Geese have exhibited lesions in the pericardial and peritoneal sacs As a rule attempts at experimental inoculation of the lower animals with pure cultures results in failure however lizards monkeys guinea pigs and some of the other experimental animals have been successfully inoculated

Actinomycosis in Man

Farmers and cattlemen are the classes most commonly diseased As a result males in the prime of life are the commonest subjects In Sanford s statistics 670 cases in the United States revealed 80 per cent in males The majority were young adults but no age group was

how they might inaugurate actinomycosis around the teeth and in the gastrointestinal tract if as and when the proper conditions for successful invasion arise

Geographic Distribution of Actinomycosis

Actinomycosis probably occurs in many parts of the world, though figures are lacking It has been reported from Europe North America and South America In the United States Sanford and Voellker collected reports upon about 570 human cases from every state in the Union The Mississippi Valley and the Northwest, however, showed the greatest number of cases

Transmission of Actinomycosis

The mere presence of vegetable fibers mostly hay and straw in 7 per cent of the tonsils of hogs and in 4 per cent of those of cows only suggests a source of infection in such vegetable matter for it is rare to demonstrate such fibers in the tissues of human actinomycosis When though the fungus is demonstrated within the fibers as has been done in the lesion it is another story The outcome of all the considerations leads to the conclusion that it is not necessary to invoke actinomycotic animals as the direct source of infection of man At the same time it cannot be denied that animals must act as passive carriers at least continuously distributing the fungus over vegetation through saliva or through feces,—whether used as fertilizer or not As in the case of coccidioidal granuloma most examples of human actinomycosis appear to be contracted from the same source in nature that animals acquire it Attempts at substantiating direct acquirement from animals have failed (Sanford Emmons)

Animals Susceptible to Actinomycosis

Cattle are outstandingly affected Thereafter man horse pig and sheep are rather frequently affected More rarely the dog goat guinea pig rabbit and goose have been concerned Among wild animals the monkey, lizard grizzly bear tapir deer llama, elephant and antelope have been reported Some of the latter were in captivity but specimens shot in the wild including stone sheep in British Columbia prove that the disease can be acquired apart from human environment The disease was found in a fossil rhinoceros in northwestern Nebraska

cattle with actinomycosis should not be allowed to pasture with other cattle because they would certainly contaminate the vegetation It is similarly inadvisable for man to chew straws weeds and grains

SPOROTRICHOSIS

This is one of the specific infectious granulomatous diseases Like tuberculosis actinomycosis and syphilis it follows a subacute indolent course characterized by gumma like lesions and ulceration—naturally with variations

Whereas for man no less than ten species have been described only one of them namely *Sporotrichum schencki* is of importance for animals It has been isolated in France from several forms of vegetation (beech oat grains and shave grass) (8) Ample clinical evidence incriminates punctures by rose and barberry thorns (9) Carnation and rose buds have been successfully infected and retro cultures from them have produced sporotrichosis in experimental animals It is thus clear that the species is widely distributed upon vegetation thus affording the opportunity for direct infection of both man and lower animals Man has been infected following the bite of the rat mule dog chicken mosquito and horse but since similar infection has followed injuries by splinters and contact with rotten sticks when clearing land it is not just to condemn those animals without qualification they may act only as passive porters

Sporotrichum schencki is extremely difficult to demonstrate in pus or other tissue cultural methods are mandatory Fortunately it grows easily In tissues it is an ovoid yeast like cell of the dimensions of bacteria whereas in culture only mycelia and conidia are developed

The fact that it produces agglutinins that are highly specific is almost unique in mycology Spores secured from young colonies filtered through cotton serve as the antigen They may be agglutinated in dilutions of 1 1500 up to 1 4000

Sporotrichosis in Man

This begins as a solitary granulomatous lesion on some exposed part of the body—usually on the hand or forearm but also on the lower extremities or the face The eyelids may become diffusely involved leading to the mistaken diagnosis of trachoma and lesions on the side of the nose have been erroneously regarded as due to dacryocystitis

immune The *youngest case was an infant 28 days old and there* were 22 others less than ten years old Two patients were 82 years old

The mode of infection is usually in doubt Ewing collected records of 100 cases in the United States in 1902 and could find no evidence of an infection from animal to man either through milk or meat or by accidental inoculation It is probable however that persons who suck or chew straws grains or weeds lay themselves open to infection the presence of a carious tooth or an abrasion would *facilitate entrance of the inoculum* Cereal grains *are capable of* penetrating soft tissues thus carrying in the infectious matter Cutaneous infection has been caused by wood splinters

As in cattle, the jaw is the commonest location however an osteitis is practically unknown at least in the United States It is the surrounding fibrous parts that are affected The mass is diffuse comparing with cancer in its wooden hardness and is comparatively painless The surrounding skin is dusky red to violaceous Progress is slow the enlargement occurring by fits and starts The multiple *granulomas in the depths of the mass coalesce suppurate* and discharge upon the surface by sinuses However the abscesses in the depths are not adequately drained The pus which escapes contains the well known sulphur granules easily visible to the naked eye Regional lymph nodes although they may become swollen do not contain granulomas and discharge pus this is an important differential diagnostic distinction from actinobacillosis in which such nodes are regularly involved

Generalization (2 per cent of cases) is delayed for many years but eventually may become widespread—both by direct continuity of tissue and by the blood stream Secondary to intestinal and particularly appendiceal involvement the skin over the abdomen may become involved by direct extension The same is true of pulmonary lesions which extend to the skin of the thorax Primary actinomyco*sis of the skin is excessively rare (about 2 per cent)*

The symptoms may thus simulate syphilis tuberculosis sarcoma carcinoma or mycetoma The prognosis is bad unless actively treated in the earliest stages generalized cases are invariably fatal but only after a long drawn out course i e up to fifteen years

Prevention of Actinomycosis

Since *Actinomyces bovis* is evidently widespread upon grasses and grains there is little that can be done in prevention However

cattle with actinomycosis should not be allowed to pasture with other cattle because they would certainly contaminate the vegetation It is similarly inadvisable for man to chew straws weeds and grains

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The lesion grows rather rapidly attaining the size of a small marble in 2 or 3 weeks It is firm purplish red and painless At about the fourth week it ruptures and develops into an ulcer It thus suggests a furuncle but one which is not violently inflammatory and which does not heal after rupture Lesions of this sort should always prompt thoughts of sporotrichosis

At times such a lesion may remain solitary but in America secondary lesions generally develop, distributed along the perivenous lymphatic channels This leads to a tract of older and younger granulomas numbering up to 20 or 30 While they may extend quite to the regional lymph nodes the latter are themselves involved with the utmost rarity Such a picture is almost pathognomonic

The patient remains in good general health and solitary lesions have been known to heal spontaneously but usually the course of the disease is indefinite unless treated Fortunately iodides are specific Only 3 of 148 cases reported in the United States were fatal Blood stream invasion occurs late and uncommonly but once generalization occurs any or all viscera are liable to involvement When tuberculosis is associated the two diseases appear mutually to aggravate each other

Sporotrichosis in Animals

Sporotrichosis affects animals only sporadically—rats horses mules and dogs Of these Norway rats are the more frequently concerned cheesy nodules appearing on the tail and paws and producing a swelling of joints with deformity At times granulomas also appear in the viscera In dogs the features are similar to those of man with emphasis upon the bones and joints peritonitis secondary to hepatic involvement may be associated In horses and mules too the disease is like that of man with a more or less linear lymphangitic distribution on the extremities again without metastasis to the lymph nodes Exceptionally the nasal mucosa suffers It resembles epizootic lymphangitis but runs a much milder course

Experimentally rats and monkeys are easily infected Incidentally a species of Sporotrichum which was close to *Sporotrichum biparasiticum* was isolated from well water in Algeria and was pathogenic for the monkey (*Macacus rhesus*) the white mouse guinea pig and rabbit This kind of a source may be of significance for other species of Sporotrichum

In all of the animals spontaneously infected *Sporotrichum*

schencki is the species etiologic except that for the dog *Sporotrichum canis* and perhaps other species have been at least quoted The data for *Sporotrichum canis* are not convincing

As to prevention injuries by vegetable matter whether directly or through the bites of animals should be avoided The ubiquity of rats involving the soiling of splinters and other sharp materials incriminates these pests in just one more connection

SUPERFICIAL FUNGOUS DISEASES

Most of the reported cases of transmission between man and animals are wide open to criticism because they are based upon such slim mostly circumstantial evidence moreover many of them are but isolated cases Such a criticism however is not unique to fungous disease There still remains a large accumulation comprised of groups of cases about which there can be no doubt and which collectively bespeak a real importance of animals in transmitting fungous disease Such cases are decidedly strengthened when supported by laboratory studies as illustrated by the experience of Roberts (11) A kitten with ringworm originating in Egypt infected a passenger en route to England In England it infected another kitten and twelve members of a family The latter kitten in turn infected a child and a dog in a neighboring house Roberts personally observed both of the cats the dog and the children At this juncture the circumstantial evidence was supported by the cultural work that he did whereby the same species of Microsporum was isolated from all three kinds of host —man cat and dog

Additional but still circumstantial data are such as those where the location of the lesions is on parts of the body which come in contact with animals Thus cases of mouse favus transmitted through a cat were located on the necks of the patients where they were accustomed to lay the cat when petting it In this particular case an additional item of significance was the fact that the cat had recently arrived from the country where mice are expected to be more numerous

Ringworm in Man (8)

Scalp ringworm in children The fungus *Microsporum felineum* of the cat has been frequently found in the lesions of children incidentally veterinarians from their side quote dogs and man as a source of cat ringworm Roberts report has been already cited

The lesion grows rather rapidly attaining the size of a small marble in 2 or 3 weeks It is firm purplish red and painless At about the fourth week it ruptures and develops into an ulcer It thus suggests a furuncle but one which is not violently inflammatory and which does not heal after rupture Lesions of this sort should always prompt thoughts of sporotrichosis

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In all of the animals spontaneously infected *Sporotrichum*

from several of the patients The disease was eczematoid and affected the hands and forearms mainly but the beard was involved in one of the patients Unfortunately cultures were not made Bazin saw five men infected from one horse and Papa reported a number of examples of transmission —horse to man man to man man to wife wife to infant Weidman has observed several cases of dermatophytosis in monkeys and apes at the Philadelphia Zoological Garden which were confirmed by finding fungus in the scrapings and in one case by culture He saw similar lesions on a chimpanzee in the zoological garden at Rome

Ringworm in Animals (10)

Herpes tonsurans (*ringworm in animals*) It can scarcely be said that there is an analogue of ringworm of the scalp beard or glabrous skin for the lower animals because in them the entire body is hairy At best one can speak only of ringworm of animals in its largest aspects Veterinarians call the disease "herpes"

For horses there is a large and valuable material reported by Brocq Rousseau and his collaborators who studied 140 cases of ringworm in French army horses Out of 92 cultures *Microsporum equinum* was found 79 times *Trichophyton equinum* 10 and *Trichophyton gypseum Trichophyton verrucosum* and *Achorion gypseum* 1 each Obviously the Microsporums predominate Subsequently Brocq Rousseau indicated that *Trichophyton verrucosum* certain *Trichophyton faviformes* and *Trichophyton asteroides* may also be causative

In cattle *Trichophyton faviforme verrucosum* var *vituli Trichophyton albicans* and *Trichophyton discoides* are quoted by Hutyra and Marek as causative *Grubyella camerounensis* of Ota was isolated from one of the African cattle of the Cameroon In the Belgian Congo *Dermatophilus congolensis* was the cause of impetigo like ringworm

In cats and dogs *Microsporum felineum* and *M canis* (*M lanosum*) are the commonest species In 3 different breeds of sheep in the Dutch East Indies ringworm apparently contracted from a child is said to have been due to *Microsporum audouini* variety *hemitragi*

Favus (8)

The feature upon which favus depends for its autonomy is its capacity to exhibit the favus cup or scutulum It is pathognomonic

above There is also little doubt that tinea capitis may also be contracted from dogs cattle and horses and there are suspicions that it may also be acquired from sheep monkeys and apes

Vaccination ringworm Three endemics of scalp ringworm were reported in Germany by Hager in 1888 The disease was at first mistaken for impetigo until a dermatologist was assigned to investigate the situation and demonstrated fungus in the lesions Altogether upwards of 1 700 children were affected Other similar endemics in Germany which followed vaccination may have been also of fungous causation but remain doubtful because examination was not made for fungus The vaccine was traced to three calves but the fungus could not be demonstrated from them

Guy and Jacob observed at least 75 cases in a Pittsburgh endemic In general the lesions developed near a vaccination site, but were also found elsewhere They isolated *Epidermophyton inguinale* which is not an organism of cattle by any means as well as a white culture which was probably *Trichophyton interdigitale* Dermatophytosis of the feet and elsewhere was present in some of these patients and Guy raised the point that possibly the lesions resulted from autoinoculation In view of the ubiquity of this disease there are possibilities that it may have been introduced into the vaccine from workers in the commercial laboratory glycerine supports fungous growth well The evidence of another Pittsburgh dermatologist Hollander to the effect that the vaccine virus in each of his cases was the product of one biologic manufacturing firm is significant moreover the fact that dermatophytosis is not commonly and consistently discovered around vaccination lesions of an American race that is ridden with dermatophytosis speaks against autoinoculation

Ringworm of the beard (tinea barbae) Of all the forms of ringworm this is outstandingly of animal origin Only cattle and horses appear to be concerned and correspondingly only cattlemen and cavalrymen are the classes which are affected The several members of the *Trichophyton gypseum* group are the commonest offenders

Ringworm of the glabrous skin The same animals fall under suspicion here as in ringworm of the scalp —cats dogs cattle, horses and monkeys There is an adequate accumulation of clinical evidence incriminating these animals well supported by laboratory studies Tilbury Fox gives a complete account wherein an old white pony was the reservoir from which seven human contacts became infected —stablemen and hospital attendants in different buildings Fungus was demonstrated in hairs from the horse and in scrapings

dogs Transmission from these animals though is only inferential

Epizootic lymphangitis This common affection of horses is due to a species of *Histoplasma* (*farciminosum*) The parasite has been known in tissue for many years but its proper classification awaited the culture which has been only recently achieved The disease in man reported only three times is similar to that of horses Granulomas perhaps ulcerative are distributed widespread over the body following the lymph vessels and nodes Mucous membranes may be affected

The result of the culture is to show that *Histoplasma farciminosum* is almost identical with *Histoplasma capsulatum* of man (12) The latter however induces an entirely different type of disease it is a generalized systemic one of the entire reticuloendothelial system which is invariably fatal (13) It still remains to be demonstrated whether the parasites of the horse and man are identical species if so another disease is classifiable among those of both man and the horse with possibilities of transmission

Histoplasmosis in mice (India and Italy) This is recorded because both the disease and parasite were analogous to those of man It cannot be claimed that the two are quite the same because the parasite has not been cultured (Shortt) (14) As in man myriads of minute rounded encapsulated bodies suggesting pneumococci occupy the reticuloendothelial cells throughout the body extra cellular ones may be budding

TORULOSIS

This is a rare disease of man caused by *Torula histolytica* It has occurred in two horses and in two cheetahs in captivity Although there are no data to prove transmission from animals to man the fact that the fungous cells have been demonstrated in urine is highly suggestive

COCCIDIOIDOMYCOSIS (CALIFORNIA DISEASE)

This disease caused by *Coccidioides immitis* has been identified far from its original locus in California it is endemic in south western United States as far as mid Texas Its acute phase has simply the significance of an acute upper respiratory infection but the chronic granulomatous one has a mortality of upwards of 90 per cent Cattle sheep and dogs of California exhibit the disease as a caseous granuloma of the midiastinal lymph nodes which is be

It is the product of a massive growth of fungous substance some times the size of a small marble but not of any particular species of fungus It forms in and around the orifice of a hair follicle the summit bearing a saucer or cuplike depression It should be emphasized however that cups are not always present

In man it is the scalp that is almost invariably affected The disease produced is essentially only a folliculitis resulting in permanent scarring and alopecia In addition to the cups there are yellow crusts the color of which may be accentuated by alcohol They have a mousy odor common to decomposing crusts in general Rather exceptionally the disease extends to any or all parts of the body in addition The latter lesions respond readily to treatment but the ones on the scalp are most stubborn Cases caused by *Achorion quinckeanum* of the mouse are decidedly rare are confined as a rule to the trunk and respond readily to treatment

In the cat (10) in addition to the ears legs and shoulders being involved there is a special predilection for the paws particularly around the claws In sheep lesions appear on the head especially around the lips and nose and on the internal ear In rabbits the head and claws are mainly affected but other parts may suffer Hares share the infection —at least once with gangrene and destruction of the eye It is questionable whether horses have been proven favic except rarely around the hoof Asses and mules rather frequently exhibit it —confined to the hoof

Ringworm species etiologic (2) For man *Achorion schonleinii* is usually concerned and there is a possibility that it can be transmitted from cats which in turn acquire it from rats *Achorion quinckeanum* infection is unquestionably acquired from mice and rats For dogs *Oospora canina* is the commonest species —*Achorion schonleinii* and *Achorion gypseum* more rarely While in mice *Achorion quinckeanum* is predominantly the cause *A violaceum* has been isolated at least once In Switzerland certain dwellings are known as "favus houses because a number of cases of human favus have originated in them and mice on the premises have been found favic Sabrazes (cited by Hutyra and Marek) has transferred favus from dog to man

HISTOPLASMOSIS

The cause of the human disease *Histoplasma capsulatum* has been found recently to have caused spontaneous disease in two

10 Torulosis has been found in man horses and cheetahs on a very few occasions

11 Coccidioidomycosis occurs in cattle sheep dogs and rodents of southeastern United States but how man is infected is uncertain

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nign The matter of transmission to man has been thoroughly investigated, with the result that the animals have been declared not guilty They acquire the disease from the same sources in nature (dust etc) that man does

The situation is different though for the small rodents of the southwestern desert country Emmons has cultured *Coccidioides immitis* (and a related fungus *Haplosporangium parvum*) from them and from soil Since upward of 97 per cent of Indian children give a positive coccidioidin test it is clear that the acute infection at least is acquired by nearly everybody in the endemic area Rodents which die and whose carcasses become disintegrated and incorporated in the soil must furnish an abundance of the infective fungous cells (chlamydospores) to the dusts of that country Inasmuch as Negroes are far more liable to the chronic (and fatal) form of the disease a certain Army directive has recommended that they be not assigned to the endemic areas (15)

ITEMS OF NOTE

1 Actinomycosis is probably not transmitted directly from animals to man Cattle and hogs may act as disseminators of the infection in nature however
2 For man actinomycosis is largely rural attacking mostly young adult males While most lesions occur on the head and neck no part of the body is free from danger
3 Milk from actinomycotic cattle is not a hazard to man provided the udder is not infected Meat is not a hazard provided the infected part is cut away
4 Sporotrichosis can be contracted by man from infected splinters of wood and from the bites of animals
5 Scalp ringworm in children is caused by a parasite of the cat but may also be spread by other animals
6 Vaccination ringworm so called has been traced to calves through vaccine virus but evidence is lacking that this method of transmission is of importance
7 Ringworm of the beard is confined largely to cattlemen and cavalrymen the only animals implicated being cattle and horses
8 Ringworm of the glabrous skin is transmitted to man from cats dogs cattle, horses monkeys
9 Histoplasmosis is a common affection of horses but the disease in man is rare

SECTION TWO

DISEASES OF RODENTS AND WILD ANIMALS

CHAPTER XIX

PLAGUE*

PLAGUE is an acute infectious disease caused by *Pasteurella pestis* Primarily it is a disease of rodents especially rats secondarily it is a disease of man The bubonic type in man is transmitted from rodents by means of infected fleas the pneumonic type spreads from man to man directly

HISTORY

During the 1 500 years before the Christian era there were forty one epidemics of plague (12) One of the early records of its ravages is recounted in the Bible (I Samuel Chapters 5 and 6) The Philistines made golden images of the mice that over ran the land in order to stay the pestilence The outbreak began at the seaport town of Ashdad and moved inland At Beth shemesh the mortality is given as 50 070

Outbreaks occurred from time to time during the ensuing centuries but records sufficiently accurate were not kept to make even the diagnosis certain Papon (12) however states there were 109 epidemics during the first 1 500 years of the Christian era and 45 from 1500 to 1720

The first authentic epidemic of plague began in 542 A D at Pelusium in Egypt This city was a leading center for trade between the East and the West The main trade routes at that time between Europe and the East were along the Mediterranean Sea and over land through Turkey Germany and France It was along these routes that the infection slowly spread till every country then known was afflicted from Asia to Ireland At the height of the epidemic the mortality was 5 000 persons daily and at times this reached 10 000 According to *Procopius* "it spared neither island nor cave

* Prepared by Karl F Meyer D V M Ph D M D Hooper Foundation University of California San Francisco Calif

auxiliary factors which have come into full force whenever the disease was imported into Europe even in recent years But in the light of knowledge collected since 1900 the decline of plague at the end of the 17th century represents an example of the great natural law of the rise and decline of epidemics



Pri t f m th Am ri n Museum f N t l Hist ry

FIG 46 —Plague among the Philistines A 17th Century conception as depicted by Nicolas Poussin Although it was nearly three hundred years later that the relation of the rat to plague was definitely established the presence of large numbers of rats is here shown

During the 18th and the early part of the 19th century plague continued to prevail in Turkey Asia Minor Syria Egypt and Greece An outbreak near Vethanka on the Volga in 1878 1879 was the last appearance of plague in Europe for 17 years

The last pandemic with which all important parts of the world became concerned is supposed to have originated in China in the province of Yunnan on the Thibetan border in or around 1871 1877 moving in an easterly direction reaching Canton and Hong Kong in May 1894 The deaths in Canton have been estimated at between 80 000 to 100 000 During the epidemic in Hong Kong the causal agent of plague *Pasteurella pestis* was discovered by S Kitasato (10) on June 14 and independently by Yersin (27) on June 20 1894 The South China ports of Canton and Hong Kong infected

nor mountain top where man dwelt Many houses were left empty and it came to pass that many from want of relatives or servants were unburied for several days At that time it was hard to find anyone at business in Byzantium Most people met in the streets were carrying a corpse All business had ceased All craftsmen had deserted their crafts After about two hundred years the epidemic subsided

The second pandemic of plague known as the Black Death originated in Mesopotamia about the middle of the eleventh century attained its height in the fourteenth century and did not disappear till the close of the seventeenth century It is thought that the Crusaders, returning from the Holy Land in the twelfth and thirteenth centuries were instrumental in hastening the spread of the disease Trade routes were primarily involved the infection spreading to the East the West and the North over the then civilized world During the course of the disease 25 000 000 people perished one fourth of the world s population

Towns were left empty and all trade was at an end for none knew when his turn to be smitten would come In London in 1664 and 1665 in a population of 500 000 there were 70,000 deaths from plague

Shortly thereafter plague rapidly disappeared from the whole of Western Europe The last epidemics were in Ireland in 1650 Denmark 1654 Italy 1657 Spain 1677 1681, and in Eastern and Southern Germany in 1679 1681 It is indeed a remarkable epidemiological fact that in such a short time plague should entirely disappear Various explanations have been offered to assess the reasons for the retrogression of plague from the West Progress of civilization in particular the control of epidemic diseases by social defense in form of sanitation housing and cleanliness and the supervision of the infectious sick were considered important factors Liston (11) connected the disappearance of plague with a change in the rat population In particular, the agrarian revolution led to the exclusion of rats from human dwellings and thus favored the substitution of one species of rat for another On the other hand with the abandonment of the old trade routes the transfer of commercial activity to Amsterdam and London whose connections with the Far East were by sea and not by land reduced the opportunities of renewal of the disease by fresh invasion (Simpson) Neither of these theories offers a fully satisfactory explanation They were doubtless important

As the epidemic increased in magnitude commissions appointed by various European Governments proceeded to India working especially in Bombay Of importance are the reports by the Austrians (1898 1900) the Germans (1899) and the Russians (1897) The Advisory Committee appointed in 1905 by the Secretary of State for India the Royal Society and the Lister Institute published a long and very valuable series of Reports (1906 1917) which advanced greatly the knowledge of the ecology

Reference to the relationship of rat mortality to plague was first noted in India in 1837 From the time of the Canton epidemic plague in rats has been found in the majority of epidemics Spontaneous plague was also found in other rodents such as tarabagans squirrels gerbilles and mice but the rat was the principal animal incriminated The mechanism of transmission of the plague bacillus from rat to man became only gradually apparent Ogata (1897) and later Liston (1905) advanced the theory that the transmission occurs through fleas The subject was thoroughly investigated by the Advisory Committee and the actual means by which the plague fleas transmit the bacillus was investigated by A W Bacot and C J Martin in 1914

THE ETIOLOGIC AGENT

Pasteurella pestis commonly known as the *Bacillus pestis* is a member of the group of bacteria which cause haemorrhagic septicemias (pasteurelloses) of various animals Morphologically it is a rod 0 5 to 0 7 microns wide by 1 5 to 2 0 microns long which is gram negative but shows bipolar staining and thus appears as safety pin like forms singly or in pairs In tissues it may be quite pleomorphic globular and club shaped poorly stainable forms are by no means uncommon The bacillus is non motile and does not form spores A capsule like envelope is readily demonstrable on virulent strains Growth takes place readily upon ordinary culture media and is slightly better at 30 than 37 C Addition of cystine blood or sodium sulfite improves the growth which is always slow in appearing Distinctly visible colonies appear after 24 hours the growth may be quite stringy Milk is never coagulated acid is produced in glucose maltose and mannite and no indol formed The resistance to dessication sunlight and disinfectants is slight *P pestis* may be readily agglutinated by specific antisera and thus differentiated from other organisms with which it may be confused

with plague became the distribution center Sea going ships conveyed the infection over the seas to India, Australia Japan and the Americas The precise date and manner of the arrival in Bombay is unknown not until September, 1896 was plague suspected irrespective of the fact that rats were dying in numbers Unfortunately no particular importance was attached to this important phenomenon at that time



From an old print furnished by the American Museum of Natural History

Fig 47 —An ancient conception of the cause of plague showing the angel of death wreaking vengeance on the populace

In the course of twenty years plague spread from India to Singapore the Philippine Islands Arabia Persia Turkey Egypt South Africa Madagascar North and South America Central America the West Indies and Mexico Nearly every country became affected a distribution indeed dissimilar to that of any former epidemic of plague India became the scene of an appalling epidemic Mortality records gave the reported plague deaths between 1896 and 1917 as 9 841 396 with a maximum in 1907 of 1 315 892 or a rate of 5 16 per thousand of the population Fortunately during the past twenty five years there has been a tendency toward greatly diminished prevalence In 1923 there were not over 250 000 deaths and in 1941 only about 4 212 cases but during the first half of 1945 the figure rose again to 18 088 cases

Plague at present maintains its worldwide distribution of active endemic foci largely due to epizootics among rats The unevenly scattered foci of *murine plague* enhance the danger that maritime exchange along the lines of travel may introduce the infection into new territories Fortunately there are recent findings which would tend to give some assurance that this spread by sea and even land routes has been greatly diminished

(a) Plague during the past ten or fifteen years has tended to establish its endemic home in the cooler hinterland rather than in the ports of warm countries

(b) Since 1929 the number of plague infected vessels arriving from ports continuously infected such as Rangoon Colombo and Bombay is quite negligible no vessels so infected were reported be tween 1936 and 1940

(c) Rat populations on ships have been considerably reduced through rat proofing methods

(d) Improved procedures adopted in ports exclude the transport of rats in cargo and fumigation with cyanide of all grain and con tact cargoes as for example in Ceylon eliminates the infected fleas

The most important plague foci are in India and China Infection is also found throughout Eastern Asia In Burma plague was much more severe in 1938 than in any of the preceding ten years There has been a heavy rise in incidence in Thailand An outbreak oc curred in New Caledonia (1941) in Egypt and in Senegal Morocco and Tunis Since 1911 the Netherlands India plague has caused no fewer than 211 000 deaths some areas have been freed from rats and plague by a systematic reconstruction of thousands of villages An old plague focus on the Island of Hawaii is again active

The great pneumonic plague outbreak in Manchuria 1910 1911 with a mortality of over 60 000 deaths and a smaller epidemic of 10 000 deaths in 1920 1921 has been attributable to the existence of sylvatic plague in the wild rodents in particular the tarabagan in outer Mongolia Studies incident to these epidemics have focused attention on the unknown problems of sylvatic plague It is now recognized that in South Africa Southeast Russia Transbaikalia and possibly in Argentina—the endemic *rural* plague regions—a par ticular fauna represented by the rodent species belonging to the *Sciuridae* or *Gerbillinae* living in subterranean colonies in families or singly maintains the exchanges of the plague bacillus A group of small rodents (varieties of *Muridae Cricetidae* and *Jaculidae*) and

Conclusive evidence of the presence of *P pestis* in tissue material sputum and ectoparasites may be obtained by subcutaneous inoculation or by rubbing such material on the freshly shaven scarified skin of guinea pigs The anatomical lesions produced are quite characteristic and therefore this animal is most useful in the diagnosis of plague Experimental work on plague also makes use of the high susceptibility of certain strains of white mice or sometimes black rats and rabbits

GEOGRAPHIC DISTRIBUTION AND PREVALENCE

According to Robertson of the United States Public Health Service Bubonic plague is essentially a disease of hot climates and having been introduced into tropical countries it tends to persist indefinitely Outside the immediate tropics this disease is rather definitely limited in the extent to which it will spread

In countries with a mean midwinter temperature of 45°F or below bubonic plague is occasional accidental and distinctly self limited and it seems possible for it to occur in the colder regions only for short periods under unusual conditions

Central Asia is reputed to be the original home not only of the human race but also of plague That area has been a perpetual focus of infection and from Asia bubonic plague has followed man *in his trade and commerce to almost every country in the world* All of the pandemics have been traced to that source Other foci of infection have appeared however which are potential sources of danger Wu Lien Teh (26) (table 33) has listed such endemic foci

The most important areas as far as serious outbreaks are concerned are Kurdistan and the region around the Himalayas Thibet Yunnan and Kumaon

Table 33—Foci of Plague Infection

	Earliest Known Infection
Africa	
Benghazi	1270
Central Africa	1864
Asia	
Arabia	1157
Kurdistan	Oldest records
India (Kumaon)	1823
China (Yunnan)	1853
Mongolia	1856
Thibet	1900
Turkestan	1884
Persia	1876
Astrakhan	1364

tance is the permanent endemic *sylvatic* or *rural plague* area which extends from the West Coast into North Dakota and Kansas and from the Mexican border in the South to the Province of British Columbia and Alberta in the North (Figure 50) While investigating the origin of a case of fatal plague in 1903 Rupert Blue became impressed by the possibility that ground squirrels might be infected with *P pestis* But not till 1908 was proof obtained that mass mortalities among these rodents are definitely caused by plague Occasional human infections have been traced to contact or bites from ectoparasites of squirrels Unfortunately in 1919 a small outbreak of pneumonic plague in Oakland (13 cases) and a similar epidemic in Los Angeles in 1924 were traced to squirrel sources Until 1934 plague had been identified in only 9 counties in California With the discovery of an epizootic among ground squirrels in the Sierra Nevada mountains and in the most northeasterly county of California and with a human case in the Great Basin in Oregon intensive surveys in the western states led to the discovery of sylvatic plague or infection among at least 38 wild rodents in 14 states (see table 35) It not only exists on the eastern slopes of the Great Divide but extends into the plains east of the Rocky Mountains The apparent spread of the zone of plague infection may be due largely to intensified search and to the examination of infected ectoparasites Sylvatic plague occurs among wild rodents in wooded or rural districts uninhabited or only sparsely settled by man thus human contact with the infective agent is probably established in exceptional instances There must be an inherent weakness in the link formed by the flea which is responsible for the very infrequent occurrences of human cases on the North American continent under the conditions prevailing during the past 12 years (table 34) Uncontrolled wild rodent populations freely exchange their ectoparasites with rats and it is not unlikely that the sporadic cases of plague in the West are either contact infection through rodent bites soiling of the hands while skinning squirrels or through exposure to ectoparasites of rats and mice The relative rarity of domestic rats in the intermountain region or the active sylvatic plague areas in California may account for the absence of human plague in the midst of epizootics where pastures are littered with cadavers of squirrels proved to be plague infected and the burrow openings are teeming with infected fleas The importance of sylvatic plague as a reservoir of human disease deserves continuous investigation

occasionally representatives of the family *Leporidae* act as complementary and intermediate hosts In Russia a *Citellus* is accompanied by a *Microtus*, and in South Africa the gerbille (*Tatera lobengulae*) is joined by the multimamate mouse (*Mastomys coucha*) Human cases become numerous when the *Muridae* bring the infection close to human habitations, or a pneumonic plague secondary to bubonic plague may initiate an aerogenic dissemination

Plague is endemic in Brazil Peru Bolivia and Argentina As a rule it is relatively benign but outbreaks of pneumonic plague causing rapid contact infections among hospital nurses attendants and doctors have been observed as late as 1939 (Murdock) The most comprehensive and authoritative report on the History of Plague in the Americas has been published by Moll and O Leary (1940 1941)

In the United States plague was first recognized in San Francisco in 1900 Probably there is no more stirring account of the early efforts of sound public health and the opposition to it by the press citizens and courts than the correspondence dealing with this plague situation published in the Annual Report of the Supervising Surgeon General of the Marine Hospital Service of the United States for the fiscal year 1900 Up to 1904 when San Francisco was declared free from plague 121 cases with 113 deaths were acknowledged and reported Abundant epidemiological evidence associated rats with the outbreak A second outbreak involving 159 cases with 77 deaths occurred between May 1907 and November 1908 Infected rats as high as 2 per cent were found in badly infected districts of the city Plague infected rats were found in 1912 in Seattle and in 1914 in New Orleans In the latter city in 1914 30 human cases and in 1920 25 cases with 11 deaths were recognized At the same time Florida and Texas reported human plague (total 41 cases) *Effective suppressive measures have apparently eliminated rat plague* until recently when infected rats were again discovered in 1941 in the San Francisco Bay area and in 1943 and 1944 in Tacoma Washington Whether these findings may indicate recrudescences in old foci, or are the result of re introduction of the infection has not been determined Murine plague plays a negligible role in the United States but the risk of ports becoming infected continues to exist As late as 1943 a ship with infected rats docked in the port of New York Between *1924 and 1945 there have been no outbreaks of human plague of murine or urban origin* However of greatest impor

occupation play no role in susceptibility but Naidu (17) has shown that in India the Hindus are more liable to succumb to plague than the Parsees Jews and Europeans



F m hibit n th Am r n M m f N l Hist ry N w Y k

FIG 48 —Section of tenement house showing conditions that favor the breeding of rats

The seasonal prevalence of the bubonic type of plague depends largely upon the influence of the weather on the breeding of rats and rat fleas The Indian Commission found that in temperate regions outbreaks occurred chiefly during the summer months In hot dry climates on the other hand it flourished during the winter season dying out in summer Rats breed throughout the season in temperate climates but breeding is retarded in extremes of heat or cold With the influx of young susceptible rats the epidemic may flare up again Similarly breeding of rat fleas is retarded in the very cold or very hot months Heat interferes not only with the deposition of eggs but also prevents the eggs from developing into larvae A temperature of 85 F causes the plague bacillus to disappear from the stomach of the infected flea rather rapidly A temperature of 70 F is optimum for the propagation of an epidemic

Brooks (2) of the Indian Commission summarized his findings as follows

Table 34—HUMAN CASES OF BUBONIC PLAGUE IN THE UNITED STATES

YEAR	CALIFORNIA	LOUISIANA	TEXAS	FLORIDA	WASHINGTON (STATE)	OREGON	UTAH	NEVADA	TOTAL
1900	22	—	—	—	—	—	—	—	22
1901	26	—	—	—	—	—	—	—	26
1902	35	—	—	—	—	—	—	—	35
1903	17	—	—	—	—	—	—	—	17
1904	10	—	—	—	—	—	—	—	10
1907	170	—	—	—	7	—	—	—	177
1908	7	—	—	—	—	—	—	—	7
1909	1	—	—	—	—	—	—	—	1
1910	2	—	—	—	—	—	—	—	2
1911	3	—	—	—	—	—	—	—	3
1913	2	—	—	—	1	—	—	—	3
1914	—	30	—	—	—	—	—	—	30
1915	1	1	—	—	—	—	—	—	2
1916	—	—	—	—	—	—	—	—	0
1917	—	—	—	—	—	—	—	—	0
1918	—	—	—	—	—	—	—	—	0
1919	1	12	—	—	—	—	—	—	13
1920	1	7	31	10	—	—	—	—	49
1921	1	—	—	—	—	—	—	—	1
1922	1	—	—	—	—	—	—	—	1
1923	1	—	—	—	—	—	—	—	1
1924	41	—	—	—	—	—	—	—	41
1925	—	—	—	—	—	—	—	—	0
1926	—	—	—	—	—	—	—	—	0
1927	1	—	—	—	—	—	—	—	1
1928	3	—	—	—	—	—	—	—	3
1929	—	—	—	—	—	—	—	—	0
1930	—	—	—	—	—	—	—	—	0
1931	—	—	—	—	—	—	—	—	0
1932	—	—	—	—	—	—	—	—	0
1933	1	—	—	—	—	—	—	—	1
1934	2	—	—	—	—	1	—	—	3
1935	—	—	—	—	—	—	—	—	0
1936	3	—	—	—	—	—	1	—	4
1937	1	—	—	—	—	—	—	1	2
1938	—	—	—	—	—	—	—	—	0
1939	—	—	—	—	—	—	1	—	1
1940	—	—	—	—	—	—	—	—	0
1941	2	—	—	—	—	—	—	—	2
1942	1	—	—	—	—	—	—	—	1
1943	1	—	—	—	—	—	—	—	1
1944	—	—	—	—	—	—	—	—	0
1945	—	—	—	—	—	—	—	—	0

EPIDEMIOLOGY AND ECOLOGY

Plague is primarily a disease of rodents and man only accidentally enters into the chain of transmission The dissemination from rodent to rodent from rodent to man and possibly from man to man is accomplished by fleas Epidemics in man usually of the bubonic form include always a small number of septicemic cases and cases of secondary plague pneumonia which may by aerogenic transfer give rise to the most fatal of all infectious diseases Age sex and

plague in domestic rats and in wild rodents From an ecologic standpoint this distinction is not always easy since chipmunks or other wild rodents may invade human habitation and thus assume a domestic habitat Spontaneous plague has been observed in representatives belonging to the order *Rodentia* The rodents involved in the pandemic plague outbreaks are restricted to the family *Muridae* Although over 1 300 species and varieties are known only three *Murinae* are of universal importance

Murine or Rat Plague—The three rats largely responsible for propagating plague are the Norway or brown rat (*Rattus norvegicus*) the Alexandrian or roof rat (*Rattus rattus alexandrinus*) and the English black rat (*Rattus rattus rattus*) All three of these animals are found over the world often living together The Norway rat is the largest living in the ground under the floors and driving the other rats to the upper stories He is sometimes found on shipboard on the ground he is at home where he flourishes exceedingly outnumbering the other species in propagation He is a migrant often traveling many blocks in a night and several miles in a few days The black rat and roof rat find suitable quarters either on land between the walls or in the upper floors of buildings in trees fences and rock piles or on shipboard between walls and in cargo and merchandise

The black rat *Rattus rattus rattus* is rare in Europe today but widespread and common in the tropics *Rattus rattus alexandrinus* has been important in the epidemiology of plague in Egypt and may play a role in the Pacific Islands *Rattus hawaiiensis* in the Hawaiian Islands and the house rat *Rattus rattus griseicenter* in Java are proven plague reservoirs

Rats do not exhibit marked symptoms of plague till near death In the natural state they are said to stagger and be easily captured in cages they may seek a dark corner and try to hide

The diagnosis of plague in rats is ordinarily based upon macroscopic examination of the gross lesions which are so characteristic as to leave small doubt in the mind of an experienced observer In an epizootic however about 50 per cent of infected animals will show lesions which are so indefinite that microscopic examination or guinea pig inoculation must be resorted to

Typical lesions in acute plague are given by Williams (24) as five in number not all of which will be present at the same time neither will any one usually appear alone They are injection bubo

(1) Plague does not maintain itself in epidemic form when the temperature rises above 80°F accompanied by a saturation deficiency of over 0 30 of an inch

(2) Plague epidemics are rapidly brought to an end in the presence of a high saturation deficiency even when the mean temperature throughout and after the termination of the epidemic has been considerably below 80 F

(3) Plague epidemics may commence to increase in intensity when the mean temperature is well above 80°F provided that the saturation deficiency is below 0 30 of an inch

(4) In some districts in India and in certain tropical islands (e g Java Mauritius) where the climatic conditions are at all times of the year favorable to the incidence and spread of plague the disease may occur indifferently at all seasons

Meteorologic conditions likewise exert a great influence upon the type of plague disease which may be produced in man The severe epidemics of primary pneumonia have occurred during periods of constantly low temperature and high relative humidity Overcrowding unsanitary conditions and in Los Angeles intimate exposure at a funeral favoring droplet transmissions have been contributory factors Secondary plague pneumonia occurring as a complication of bubonic or septicemic plague are not as infectious as the primary *pneumonic plague* and unless the *conditions for aerogenic* transmission are favorable they rarely initiate large epidemics In Egypt pure pneumonic plague is rare while in Manchuria and Ural with the colder climate the primary pneumonic type is much more common Bubonic and pneumonic plague are caused by the same microorganisms but the portal of entry of the two forms of infection is distinct Epidemiologically and clinically pneumonic plague is a disease different from bubonic plague

Transmission of plague to man is commonly through the agency of fleas although other means have been recognized The bacilli may enter through the abraded skin of the feet as in cow dung-floored houses in India or of the hands of hunters handling or skinning infected animals Epidemics of bubonic plague are preceded by or associated with epizootics in rats or other rodents The great animal mortality so created favors the migration of the fleas to man The heterogeneous infection chain thus consists of (1) the animal host or carrier and (2) the vector

Plague Hosts and Carriers—A distinction is justly made between

The susliks or sisels (*Citellus pygmaeus*) in Southeastern Russia has been the subject of remarkable intricate ecological studies by Russian investigators who have succeeded in reducing these rodents to about a third and thus accomplished a liquidation of the plague epizootics (Ioff) In the veldt of South Africa extending into West Africa the gerbille (*Tatera lobengulae*) and the multimammate mouse (*Mastomys coucha*) in a complex interplay maintain plague in endemic foci Rearing of guinea pigs (*Cuis Cavia aperea*) in houses brings plague to the Indians of Ecuador and the same rodent is involved in the sylvatic plague areas of Argentina Until 1934 the ground squirrel (*Citellus beechyi*) was alone considered of practical importance in California Since then numerous species of *Citellus* marmots and prairie dogs (*Cynomys* sp) and even hares and rabbits have been encountered with spontaneous *P pestis* infections These representatives of the *Sciuridae* and *Leporidae* preside over the exchange of the infective agent while a group of small rodents belonging to the *Murinae* act as complementary and auxiliary hosts (see table 35) They support the epidemicity and may perhaps aid in the dispersion of animal plague Relatively little is known concerning this complex ecological interplay which forms the key to the solution of the plague problem in the United States There is ample evidence that transition of plague from the wild to domestic species has occurred (Los Angeles 1924) A proper evaluation of the inherent potentialities of the widespread sylvatic plague areas cannot be made until the natural histories of the rodents and their ectoparasites in the exchange cycle of the plague bacillus is definitely understood



Fig 49—Ground squirrel (*Citellus beecheyi*) reservoir of plague in the United States

Plague in ground squirrels presents a somewhat characteristic pathology The lesions of both acute and subacute or chronic infections differ from those in rats In the acute type a haemorrhagic caseous bubo is the prominent lesion while in the subacute or

granular liver, large dark spleen and pleural effusion Injection of the subcutaneous blood vessels indicated by a dusky red color of the subcutaneous structures and muscles occurs in about 75 per cent of infected animals Buboes in the rat are very suggestive of plague They may occur in the axilla neck groin or pelvis In India 75 per cent of rats with single buboes had them in the neck while in San Francisco 75 per cent of such rats had buboes of the groin The proportion of total rats with buboes varies markedly In India 80 per cent of animals showed such lesions in San Francisco 40 per cent in New Orleans 33 per cent A granular liver with focal necrosis is present in 60 to 70 per cent of all acute cases An enlarged spleen is sometimes difficult to determine as the size of the normal spleen often varies markedly but different investigators consider this lesion present in 60 to 70 per cent of infected rats Pleural effusion often copious in amount is present in more than 75 per cent of the instances usually accompanied by one or more of the other lesions A chronic form may be evidenced by very slight lesions consisting of purulent or caseous foci occurring as abscesses of the liver spleen or mesenteric glands The plague bacilli may be very scanty in such lesions and often cannot be demonstrated except by guinea pig inoculation Plague in rats suffering from the chronic form recovering from the disease can usually be suspected only by the scars present on the various organs The role of such animals in the recurrence of an epidemic is still a matter of conjecture Williams and Kemmerer (25) showed that plague without lesions occurred in rats of New Orleans and Galveston other workers in India showed that the same condition obtained in the rats of that country

Natural immunity to plague is found in many old rats The Indian Commission found 59 per cent immune to subcutaneous inoculation of material from the spleen of infected rats In San Francisco 50 per cent of large rats and 15 per cent of small rats were found resistant to inoculation of virulent material This immunity is natural and not acquired through previous attacks of the disease

Plague in Wild Rodents or Sylvatic Plague —Over 80 different species are known to be spontaneously infected with plague which not infrequently assumes the role of a seasonal epizootic affecting the younger members of the regional wild rodent population Of importance as reservoirs of plague the following may be mentioned In Mongolia and Transbaikalia the big marmot like rodent the tarbagan (*Arctomys bobac*) with a long hibernating period is important

chronic form a purulent bubo is found sometimes with purulent foci in the spleen and lungs

Spontaneous plague is rarely found among animals other than rodents Brown monkeys (*Macacus radiatus*) have suffered out

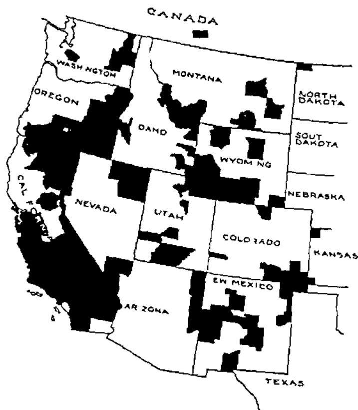


Fig 50 – Extent of sylvatic plague in the United States and Canada (to June 1944) as demonstrated by examination of squirrels marmots prairie dogs etc and their ectoparasites (Meyer)

breaks in India Shrews dogs and certainly cats may pass the plague bacillus to man Likewise ferrets (*Putorius furo*) the suricate (*Suricata*) and the yellow mongoose (*Cynictis penicillata*) are liable to acquire plague The role of the camel in the spread of the infection in Southeast Russia is not definitely established Experi

Table 35.—Wild Rodents and Rabbits of the Western United States Found Plague Infected According to K. F. Meyer 1941 5

- Order Rodentia
  - Family Sciuridae
    - Genus *Citellus* Ground squirrels
      1. *Citellus armatus* Uinta ground squirrel (1935)
      2. *Citellus beecheyi beecheyi* California ground squirrel [1908 (>2500)]
      3. *Citellus beecheyi douglasii* Douglas's ground squirrel (1941)
      4. *Citellus beecheyi fisheri* Fisher's ground squirrel (1937)
      5. *Citellus beldingi oregonus* Oregon ground squirrel (1934)
      6. *Citellus columbianus columbianus* Columbian ground squirrel (1938)
      7. *Citellus columbianus ruficaudus* Blue Mountains ground squirrel (1938)
      8. *Citellus lateralis chrysodeirus* Golden mantled ground squirrel (1937)
      9. *Citellus richardsonii elegans* Wyoming ground squirrel (1937)
      10. *Citellus richardsonii nevadensis* Nevada ground squirrel (1937)
      11. *Citellus richardsonii richardsonii* Richardson's ground squirrel (1935)
      12. *Citellus variegatus grammurus* Say's rock squirrel (1936)
      13. *Citellus variegatus utah* Utah rock squirrel (1936)
      14. *Citellus washingtoni loringi* Loring's ground squirrel (1938)
      15. *Citellus washingtoni washingtoni* Washington ground squirrel (1938)
      16. *Citellus townsendii*, Tinto ground squirrel (1942)
    - Genus *Tamiasciurus* Red squirrels
      17. *Tamiasciurus douglasii albolimbatus* California chickaree (1937)
    - Genus *Glaucomys* Flying squirrels
      18. *Glaucomys sabrinus lascivus* Sierra flying squirrel (1937)
    - Genus *Eutamias* Western chipmunks
      19. *Eutamias speciosus frater* Tahoe chipmunk (1936)
    - Genus *Cynomys* Prairie dogs
      20. *Cynomys gunnisoni zuniensis* Zuni prairie dog (1938)
      21. *Cynomys leucurus* White-tailed prairie dog (1938)
      22. *Cynomys parvidens* Utah prairie dog (1936)
    - Genus *Marmota* Marmots
      23. *Marmota flaviventer engelhardti* Engelhardt marmot (1936)
      24. *Marmota flaviventer nosophora* Golden mantled marmot (1937)
      25. *Marmota flaviventer flaviventer* Yellow bellied marmot (1942)
  - Family Geomyidae
    - Genus *Thomomys*
      26. *Thomomys bottae* Western pocket gopher (1942)
  - Family Heteromyidae Kangaroo rats and pocket mice
    - Genus *Dipodomys* Kangaroo rats
      27. *Dipodomys ordii ordii* Ord's kangaroo rat (1939)
  - Family Cricetidae Native rats and mice
    - Genus *Onychomys* Grasshopper mice
      28. *Onychomys leucogaster* Grasshopper mouse (1943)
    - Genus *Peromyscus* White footed mice
      29. *Peromyscus truei gilberti* Gilbert's white footed mouse (1934)
      30. *Peromyscus truei truei* True's white footed mouse (1934)
    - Genus *Neotoma* Wood rats
      31. *Neotoma cinerea occidentalis* Western bushy tailed wood rat (1934)
      32. *Neotoma fuscipes mohavensis* Mohave desert wood rat (1934)
      33. *Neotoma lepida intermediate* Wood rat (1934)
      34. *Neotoma lepida lepida* Desert wood rat (1935)
    - Genus *Microtus*
      35. *Microtus californicus* Meadow mouse (1942)
  - Family Muridae
    - Genus *Rattus* Rats
- Order Lagomorpha Hares and rabbits
  - Family Leporidae Hares and rabbit
    - Genus *Lepus* Jack rabbits
      36. *Lepus californicus* Black tailed jack rabbit (1942)
    - Genus *Sylvilagus* Cottontails
      37. *Sylvilagus nuttallii nuttallii* Washington cottontail (1939)
      38. *Sylvilagus sp* Cottontail (1942)

it has become infected through the ingestion of blood from a rat in the terminal stages of a *P pestis* bacteremia These individuals are capable of transmitting by the so called blockage phenomenon A few days or even longer periods after the flea has fed on infected blood clusters of plague bacilli become visible in the stomach Later the proventriculus becomes plugged by gelatinous masses of bacilli and its valvular action becomes inadequate Because of this obstruction the blood of the sucking flea cannot find its way into the stomach The esophagus containing virulent bacilli becomes distended The elastic recoil of the walls of both pharynx and gullet that results from cessation of sucking may drive back into the bite wound highly infective blood This recoil sometimes extends through a partial blockage to the posterior end of the stomach Many species of fleas however merely become infected and the blockage phenomenon is never evident Transmission by such species is by necessity limited to *mechanical* and *fecal* modes of infection Mechanical transmission is of great importance when several infected fleas are on a single host in fact the combined action of a large number of fleas is as efficient as infection by a single blocked specimen Of least importance is the fecal transmission since the pellets are viscous and unless the skin is broken plague bacilli are incapable of gaining entrance into the tissues of the rodent host Furthermore not all fecal pellets are infected with a sufficiently large number of *P pestis* capable of overcoming the inherent high resistance of many of the wild rodents

Many fleas remain infected throughout their entire life and never become blocked or they may carry plague bacilli in their intestinal tube for a long time before they become blocked This behavior of the flea to a plague infection is quite important since it may help to explain the carry over of plague from season to season in hibernating rodent populations However the importance of latent plague in the rodent host deserves consideration

The maximum life span of a regularly fed flea X *cheopis* is reported as 203 days but it is shortened to 20 to 30 days when the vector is infective and has a blocked proventriculus The resulting starvation alone cannot explain the early deaths of infective fleas entirely Longevity experiments made with normal wild rodent fleas have shown that unfed specimens live longer than blocked fleas when held under favorable conditions In this respect nest fleas in general tolerate hunger better than fur fleas Russian investigators

mentally, calves and sheep are quite susceptible; horses tolerate large doses of living *P. pestis*, but none of these animals are important in the dissemination of infection. Birds are quite generally resistant, but some share the burrows of the wild rodents and may be responsible for the dissemination of infected fleas.

The Vector.—Various fleas of the family *Pulicidae* are the third indispensable motive force essential to complete the cycle in the propagation of plague.

Fleas were experimentally shown by Simond in 1897 to be a possible agent for the dissemination of bubonic plague, either from animal to animal, animal to man, or man to man. The last Indian Commission fully corroborated this view. The ecology of the wild rodent fleas has been well studied by Ioff (9) in Russia and by Eskey and Haas (4) and Wheeler and Douglas in the United States.

Fleas feeding on an infected rat with a bacteremia of 100 000 000 organisms per cubic centimeter will at one feeding ingest 5 000 organisms which may multiply in the digestive tract and render the vector infective. The flea is not merely a passive carrier.

Comparatively few of the estimated 5 000 existing species of fleas have been found capable of transmitting plague. The most important species in regard to bubonic plague are listed in table 36.

Table 36.—VECTORS OF PLAGUE

FLEA (KNOWN TO BITE MAN)	DISTRIBUTION	RESERVOIR HOSTS	TRANSMITS PRIMARILY TO
Xenopsylla cheopis	Widely disseminated	Rattus rattus	Rats and man
Xenopsylla brasiliensis	Uganda, Kenya, Nigeria	Rats	Rats and man
Xenopsylla hawaiiensis	Island of Hawaii	Field rats	Field rats
Xenopsylla astia	India, Ceylon, Burma, Mesopotamia, Mombassa	Rats	Rats
Xenopsylla nubicus	Tropical East and West Africa	Rats	Rats
Xenopsylla eridos	South Africa	Wild rodents	Wild rodents
Pulex irritans	Nearly cosmopolitan	Man, swine, rodents	Man, rodents
Nosopsyllus fasciatus	Temperate zone of Europe and America	Rattus norvegicus	Rats
Diamanus montanus	Western United States	Ground squirrels	Ground squirrels
Rhopalopsylla cavicola	South America	Cavies	Cavies or Cuis
Ceratophyllus tesquorum	Russian Steppes	Citellus pygmaeus	Ground squirrels
Oropsylla silantiewi	Manchuria	Rodents (Tarbagans)	Rodents

The classical vector, the Indian rat flea, *Xenopsylla cheopis*, develops a high percentage of infective individuals in any group when

constant climatic condition but when off the host it is subject to considerable variations The microclimate of the subterranean burrows favors the spread of plague to the North beyond the 35 latitude which is ordinarily considered the limit for bubonic plague of rat origin Within limits or until such high temperatures are reached that death ensues regardless of the moisture content of the air the saturation deficiency is the more important of the two factors involved at low and medium temperatures the life span of the flea being directly proportional to the saturation deficiency of the air The highly efficient respiratory system of the flea is so constructed that during rest the trachea are nearly all closed and the flea is capable of retaining moisture Transportation of fleas in all kinds of cargo is frequently assured when the time of transportation is not very long and the climatic conditions such as temperature and humidity are adequate

Attention has been directed to the so called *flea index* either as the general flea" or species flea index In fact it was pointed out that the X *cheopis* infestation per rat in any given locality determines the degree or severity of an outbreak in a given area

Cragg (3) has shown that in those parts of India where plague does not exist the predominating rat flea is not *Xenopsylla cheopis* but other species In Colombo which enjoys a relative immunity from plague the common rat flea is *Xenopsylla astia* In the United States a survey by the Public Health Service showed that in New Orleans where the plague actually existed *Xenopsylla cheopis* was the predominating flea while in New York and Boston this pest appeared for only a few months of the year

The total number of fleas per rat varies with the climate the seasons and other factors In Belgaum India during July August and September which is the epidemic season 18 fleas per rat were found while in the colder non epidemic season only 4 or 5 were present In the United States in New Orleans in 1922 the average number of fleas in the winter time was about three while in the summer it mounted to nearly five In New York City the average number of fleas on 4 756 rats for a 2 year period was 0 95 with the largest number from any single rat 38

On the basis of epidemiological comparisons it is now recognized that the species rat flea index is of less importance than the number of infected fleas that become "blocked and therefore infective

infected fleas and then buried them for varying periods removing at intervals specimens for examination Although some fleas had no opportunity to feed during the winter they were found to be infected The maximum length of life observed in plague infected fleas was 396 days Wild rodent fleas as, for example *Neopsylla*

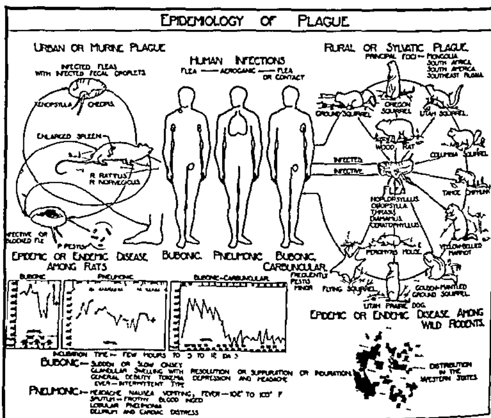


Fig 51 —Epidemiology of plague (Meyer)

setosa may readily carry the plague infection from one epizootic season to another George and Webster (6) in studying the plague conditions in the Cumbum Valley South India showed that *X cheopis* were capable of transmitting infections after the starvation up to 29 days at 79 F

The external climate temperature and saturation deficiency of the immediate surroundings of the flea determines their longevity Climatic conditions favor an abundance of rat fleas and the spread of plague The adult flea while on the host is exposed to a fairly

ture ranges from 102 to 105 F difficult and hurried breathing cough and expectoration characterize the disease The sputum at first watery and frothy is tinged with blood but rarely of viscid rusty character of that of lobar pneumonia Lung symptoms and cardiac distress increase delirium supervenes and death with the body exhibiting a cyanosed aspect (Black Death) occurs on the 4th or 5th day or earlier The pneumonic type is the most infectious and the most fatal form of plague Sporadic cases are likely to be missed and may give rise to outbreaks involving the physicians as the experiences in Oakland California in 1919 amply illustrate In the course of any bubonic plague epidemic secondary plague pneumonia may give rise to serious outbreaks during the colder seasons of the year

An early diagnosis is of greatest importance not only to the patient whose recovery may depend on an early administration of sulfadiazine and specific serum but also to his family his physician and the community because of the serious nature of the infection By puncturing the bubo in its earliest stages with an 18 gauge needle a small amount of gelatinous edematous fluid may be readily aspirated for smears and cultures In pneumonic plague the sputum usually reveals the plague bacilli in great numbers Intensive chemotherapy with sulfadiazine is the most important newer treatment of plague Important adjuvants are the injection of a potent antiserum and an adequate fluid balance Incision of buboes should be avoided until frank fluctuation occurs

PREVENTION

The control of bubonic plague is accomplished (1) by appropriate sanitary measures simultaneously directed against the rodent reservoir and the vectors (2) by protection of the individual and (3) by strict isolation of the sick and the handling of all infectious material with the greatest care

The rat population must be closely watched and any increase in rodent plague which may be detected by autopsies or by the inoculation of crushed fleas removed from the rodents must be met by adequate measures *It is impossible to estimate* the number of rats in the United States but they far exceed the human population The cost of supporting them was estimated by Creel in 1913 as $167 000 000 annually In recent years due to the general interest in rodent control work public health agencies and many citizens have

THE DISEASE IN MAN

Plague in man may manifest itself in various forms, resulting in such designations as bubonic plague pneumonic plague septicemic plague and ambulatory plague

The two chief types of clinical plague in man the bubonic and the pneumonic usually occur separately in epidemic form but occasionally the two types of epidemics may occur simultaneously as has been particularly illustrated in comparatively recent years by experience in Egypt and other parts of Africa

Bubonic plague is by far the most common type, accounting for about 75 per cent of cases It takes its name from the fact that the lymph glands draining the area through which the infection entered become enlarged (buboes) The disease is accompanied by fever depression and great prostration The enlarged lymph glands are extremely tender and painful The glands of the groin are most commonly affected because the flea bites more often occur on the legs axillary and cervical glands follow in order The incubation period varies from 2 to 10 days but usually averages 4 to 6 days The onset is sudden Mild form may be ambulatory and is usually described as Pestis minor"

The chances of recovery which may be tedious protracted or rapid are much improved after the 7th day The case fatality rate varies from 50 to 90 per cent in recent years it has been approximately 50 per cent in the United States but it was as high as 93 per cent among the inhabitants of Chinatown in San Francisco between 1900 and 1904 In rare instances complications in form of meningeal localizations may lead to late deaths In the septic variety of plague peripheral buboes are absent The patient is profoundly affected by the plague toxins which act on the central nervous system Extreme prostration with a temperature rarely above 100 F may be accompanied by nose bleeds diarrhoea etc It is always of short duration 18 hours to 3 days and invariably fatal The blood contains over forty bacilli per 0 5 c c of blood

In pneumonic plague the primary localization of the plague bacillus is in the lungs The intense congestion of the air passages with haemorrhagic exudate in the alveoli and bronchi but with little or no fibrin formation is lobular in character extending to involve entire lobes Enormous numbers of *P pestis* are always present General malaise severe headache nausea vomiting and tempera

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execute an effective suppressive program the Soviet workers used tens of thousands of workers" (Ioff) During the early years of control work in California the United States Public Health Service vaporized carbon bisulphide into the burrows of the squirrels In recent years methyl bromide has proved valuable particularly when it is accompanied by filling of burrows Later grain poisoned with thallium sulfate or strychnine as bait proved effective Experience has taught that wherever the rodent population density in canyons and draws is permitted to rise to 20 to 25 ground squirrels per acre the conditions for local epizootics are particularly favorable Control work once instituted must be continued indefinitely The natural enemies of the squirrels—the coyote wolf badger skunk hawk and mountain lion—even when little interfered with by man—have in recent years failed to exercise any appreciable influence on the reproductivity rate of the rodents and consequently sylvatic plague has assumed not infrequently the function of a check on their numbers

Flea control in houses native quarters etc should be accompanied by rodent control programs Rat harborages should be properly treated with DDT which is the pulicide of choice It may be applied as a dust or in liquid form in kerosene since it is highly effective in destroying fleas in their hiding places

In the presence of an outbreak of plague persons engaged in rat control work should be immunized and should wear flea proof clothing While repellents now available do not prevent fleas from alighting the insects leave the impregnated surface and fail to bite

Prophylactic vaccination and the injection of killed plague antigen has been advocated Various preparations have been used The available statistics have shown that they are incapable of preventing a plague infection but their use reduces the percentage of mortality The workers in India using the so called Haffkine heat killed broth culture of a highly virulent plague strain have repeatedly shown that the total number of plague cases and the death rates are lower in the injected than in the non immunized groups For example Beals (1) reported that among 6 000 unvaccinated in war in 1916 1917 there were 275 cases and 167 deaths while among 4 378 protected with Haffkine s vaccine there were only 39 cases and 10 deaths The next year among 6 000 uninoculated there were 76 cases and 47 deaths while among the vaccinated there were 17 cases with 2 deaths On the other hand these favorable results have

undertaken rat extermination campaigns by properly trained personnel Poisoning and fumigation are more effective than trapping for the destruction of large numbers of rodents Red squill phosphorous barium carbonate, zinc phosphide and thallium sulfate are the poisons commonly used Quite recently ANTU and a preparation designated as 1080 have proven more effective and may in time displace the older types of poison Experience has shown that prebaiting greatly enhances the chances of effective poisoning The chemicals are mixed with the bait and some packaged as paper torpedoes which are distributed along the runs where they are inaccessible to children and chickens In the presence of murine plague these measures must be supplemented by the destruction of rats and their fleas in the nests and burrows Cyanogas is most useful for this purpose but only specially trained personnel should apply the materials It is a light powder which releases hydrocyanic *acid on contact with moisture it is lethal to rats and fleas For* stables cellars and buildings sulphur dioxide is serviceable since it does not have the danger to human life which hydrogen cyanide does No rat control program is complete without destruction of the harborages and rat proofing of buildings Rubbish refuse and garbage which are excellent harborages must be eliminated However wooden parts in houses must be reinforced with metal to prevent gnawing through concrete stone or brick walls discourage rat harborage Screening of doors and openings around water sewer and gas pipes will prevent entry of rats In South America small flame throwers using fuel oil are employed in cleaning burrows and adobe *floors and walls*

Importation of rats from an endemic area should be guarded against by rat proofing of ships application of measures to prevent the escape of rats from the vessels as well as boarding from wharves This is accomplished by rat guards on the hawsers *In the past all* ships sailing from plague infected ports were fumigated by cyanide gas before entering a port of the United States

The suppression of plague in rural districts offers a great many difficulties Aside from the wide extent of sylvatic plague over great areas the knowledge concerning the many ecological factors which may influence the control operations is so inadequate that with the exception of a few small areas in California and according to the Russians in the Caucasian Steppes curtailment of the rodent population has not liquidated plague among the squirrels In order to

of pneumonic or suspected pneumonic plague physicians nurses and any others in contact with the patient must be protected by complete overalls gloves hoods equipped with goggles and face masks of eight layers of gauze covered by a deflection mask The chance of infection through droplets or droplet nuclei is quite high and occupational infection not infrequent When accidentally exposed to a case of unsuspected plague pneumonia the individuals must be quarantined for 7 days and chemoprophylaxis with sulfadiazine may be instituted The air of the room in which patients with pneumonic plague are housed preferably under an oxygen tent should be kept dry the use of ultraviolet light screens and possibly aerosols as auxiliary protective measures against aerogenic infection deserve consideration

ITEMS OF NOTE

1 Plague is primarily a disease of rodents
2 Bubonic plague is usually a disease of tropical or semi tropical climates
3 Pneumonic plague in epidemic form is a disease of cold and temperate climates
4 The control of rats and fleas is sufficient to control bubonic plague in man
5 Pneumonic plague lends itself to no practical control methods although chemoprophylaxis deserves consideration
6 In the United States squirrels chipmunks prairie dogs marmots pocket and white footed and meadow mice wood rats and hares are naturally infected in 14 Western States extending from the Pacific Coast to Kansas and from Arizona into the Provinces of British Columbia and Alberta
7 No practical means are available for controlling the endemic reservoir of sylvatic plague in the rural areas
8 Chemotherapy with sulfadiazine constitutes an effective treatment of human plague

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5 Fox C and Sullivan E C Public Health Reports 1925 *40* 1909 1934

not been duplicated by other workers, and the replies sent to the Office International d Hygiene Publique in 1931 1932 in answer to a questionnaire indicated that there was little confidence in anti plague vaccines prepared from killed microorganisms More recent studies only in part support this skepticism The so called United States Army vaccine is known to stimulate antibodies in those treated with 3 000 formalin killed plague bacilli It is a sound practice to repeat the injections when the population remains under exposure

As early as 1907 Strong (22) had demonstrated the value of living *avirulent plague cultures* but it was not until 1934 that Otten in Java began his careful evaluation of this method of protection In his last publication (1941) he reported that nearly ten million vaccinations had been performed In carefully controlled series in which family after family was injected alternately with 1 000 million live organisms the mortality in the vaccinated was 1 01 per 1 000 as against 4 75 per 1 000 in the non vaccinated The steady decrease of plague in Java is being attributed to the use of live vaccines Equally favorable results have been reported by Girard and Robic from Madagascar where over two million vaccinations have been performed and by Grasset from South Africa Significant statistical results are not available yet from these areas but the workers emphasize many advantages —single injections allowing mass inoculations in much shorter time comparatively little reaction and economic production because the vaccines are handled readily in the lyophile state It is important to emphasize as McCoy and Chapin did many years ago that even vaccination with live vaccine has never controlled an outbreak but it definitely reduces the mortality Pneumonic plague is apparently not influenced by vaccination Anti plague serum produced on horses with living virulent or avirulent plague strains has been recommended by Yersin (27) and others The evidence at hand shows that such sera are low in protective antibodies while sera of rabbits properly immunized are more promising There is little proof that antiplague sera possess noteworthy prophylactic properties

Human cases of plague constitute important sources of infection Strict isolation of the patients in insect proof rooms is essential The patient s clothing must be disinfected and disinfested of fleas in a steam sterilizer The wearing of gloves and gowns should be mandatory for all those who come in contact with patients In the presence

of pneumonic or suspected pneumonic plague physicians nurses and any others in contact with the patient must be protected by complete overalls gloves hoods equipped with goggles and face masks of eight layers of gauze covered by a deflection mask The chance of infection through droplets or droplet nuclei is quite high and occupational infection not infrequent When accidentally exposed to a case of unsuspected plague pneumonia the individuals must be quarantined for 7 days and chemoprophylaxis with sulfadiazine may be instituted The air of the room in which patients with pneumonic plague are housed preferably under an oxygen tent should be kept dry the use of ultraviolet light screens and possibly aerosols as auxiliary protective measures against aerogenic infection deserve consideration

ITEMS OF NOTE

1 *Plague is primarily a disease of rodents*
2 Bubonic plague is usually a disease of tropical or semi tropical climates
3 Pneumonic plague in epidemic form is a disease of cold and temperate climates
4 The control of rats and fleas is sufficient to control bubonic plague in man
5 Pneumonic plague lends itself to no practical control methods although chemoprophylaxis deserves consideration
6 In the United States squirrels chipmunks prairie dogs marmots pocket and white footed and meadow mice wood rats and hares are naturally infected in 14 Western States extending from the Pacific Coast to Kansas and from Arizona into the Provinces of British Columbia and Alberta
7 No practical means are available for controlling the endemic reservoir of sylvatic plague in the rural areas
8 Chemotherapy with sulfadiazine constitutes an effective treatment of human plague

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CHAPTER XX

TULAREMIA

TULAREMIA is primarily a disease of wild rodents especially rabbits Secondarily man is infected The causative agent is *Pasteurella tularensis*

HISTORY

Since 1910 the disease now called tularemia has been recognized under various names according to the circumstances in which it was encountered Thus McCoy designated it as a plague like disease of rodents in Utah it was known as deer fly fever and in Washington D C as rabbit fever in Idaho Lamb referred to it as "the glandular type of tick fever" and in Japan it has been reported as Ohara s disease

In 1911 (1) McCoy working in Tulare County California described a plague like disease of rodents in California ground squirrels The next year he and Chapin isolated the causative agent of the disease and named it *Bacterium tularense* (2) Both Chapin and a laboratory assistant had gone through an obscure attack of fever in the course of their work and it was found afterwards that their blood serum agglutinated this organism In the years that followed there were reported isolated instances of recovery of the tularemia bacillus from human cases

In Cincinnati three cases occurred among the patients of ophthalmic physicians In 1914 Vail described an eye infection from which Wherry and Lamb (3) isolated the tularemia bacillus this being the first human case of tularemia on record to be diagnosed bacteriologically In 1915 Sattler (4) and in 1917 Lamb (5) described similar cases of conjunctivitis

In 1920 Francis isolated the tularemia bacillus from seventeen jack rabbits and seven human cases of "deer fly fever This disease had been known in Utah since the publication of a paper by Pearse

(11) in 1911 and was so named because it was popularly supposed that infection was due to the bite of the blood sucking fly *Chrysops discalis* commonly found on horses Francis proved that the deer fly actually did transmit the tularemia bacillus He named the disease tularemia because of the presence of the tularensis organism in the blood

THE ETIOLOGIC AGENT

Pasteurella tularensis is a small rod 0 2 by 0 3 to 0 7 microns occurring singly It is non motile Gram negative and non spore bearing It is extremely pleomorphic yielding bacillary, coccoidal and bipolar forms Growth on ordinary culture media does not take place but blood agar dextrose blood agar and dextrose serum agar allows some development The addition of fresh rabbit spleen to the medium favors growth but the best media are coagulated egg yolk or blood dextrose cystine agar

The organism is easily killed by heat in ten minutes at 56 C to 58 C Cooking therefore renders infected tissue harmless Chemical disinfectants destroy the organism easily—tricresol 1 0 per cent in two minutes and formalin 0 I per cent in 24 hours Glycerin pure and undiluted is suitable for preserving spleens for laboratory inoculations the organism remaining alive many days when the spleen of an affected rabbit or guinea pig is thus treated

When such glycerinated spleens are reduced to a temperature of —14°C the time is prolonged infinitely Four strains so treated were still of maximum virulence two after a period of 13 years and two after ten years When the organs of infected animals were frozen at —14 C without glycerin the organism remained virulent for 42 months in the spinal cord 36 months in the brain 18 months in the spleen 12 months in the muscle and 6 months in the bone marrow

GEOGRAPHIC DISTRIBUTION

Tularemia has been reported from all parts of the United States (table 37) Some areas are much more heavily infected than others however In five New England States from 1929 to 1943 only twenty cases occurred and several of these were imported (21) Vermont is the only state reporting no cases of the disease

Tularemia has been reported from many other countries including Alaska Austria Canada Czechoslovakia Germany Italy Japan Norway, Russia Sweden and Turkey (table 38) The reports

Table 37—STATES IN WHICH TULAREMIA HAS BEEN FOUND TO EXIST
(With Date of First Known Cases)

State	Year	State	Year
California	1904	Oregon	1925
Arizona	1907	Pennsylvania	1925
Ohio	1908	South Carolina	1925
Utah	1908	Texas	1925
Missouri	1909	Alabama	1926
Idaho	1914	Colorado	1926
Illinois	1914	Florida	1926
Indiana	1914	Michigan	1926
Wyoming	1915	Minnesota	1926
Virginia	1920	Nebraska	1926
North Carolina	1921	Nevada	1926
Washington D C	1921	North Dakota	1927
Tennessee	1922	Oklahoma	1927
Louisiana	1923	South Dakota	1927
Montana	1923	New Jersey	1928
Mississippi	1924	New York State	1928
New Mexico	1924	Wisconsin	1928
West Virginia	1924	Rhode Island	1929
Arkansas	1925	Washington	1929
Georgia	1925	Massachusetts	1929
Iowa	1925	Delaware	1930
Kansas	1925	New Hampshire	1931
Kentucky	1925	Maine	1933
Maryland	1925	Connecticut	1940

Table 38—COUNTRIES OTHER THAN THE UNITED STATES IN WHICH TULAREMIA HAS BEEN FOUND

Country	Year	Country	Year
Japan	1925	Austria	1935
Russia	1928	Czechoslovakia	1936
Norway	1929	Turkey	1936
Canada	1930	Alaska	1937
Sweden	1931	Germany	1939
Italy	1931		

from Bulgaria covering the period 1915 to 1926 are somewhat doubtful since diagnosis was not confirmed Laboratory infections have occurred in England

SEASONAL PREVALENCE

Tularemia has no seasonal prevalence except as it is influenced by insects or by contact with infected animals Laboratory infections may occur at any time Human cases are most prevalent in summer time in the western states where ticks and deer flies are the cause of infection (*Dermacentor andersoni* March to August *Chrysops discalis* June to September) Human cases due to infection from dissecting jack rabbits are likewise most prevalent during April to October because these are the months of greatest destruction of these pests East of the Mississippi River cottontail rabbits are responsible for most human cases and since they are generally protected by law except during a few winter months the seasonal prevalence is apt to be November to January when the hunting season is on

imals killed early in the disease the first or second day after illness exhibit no gross pathologic lesions although the infection is present in the liver as well as in all other tissues of the body

Greene (19) has shown that long continued residence of *Pasteurella tularensis* in birds tends to lower the virulence of the organism Guinea pigs inoculated with strains isolated from naturally infected grouse lived for fifteen days while guinea pigs inoculated with rabbit strains lived for only six days The grouse strains passed through guinea pigs increased in virulence equal to the rabbit strains

SOURCES OF HUMAN INFECTION

There are twenty methods according to Francis (12) by which man may be infected with tularemia

Rabbits Cottontail rabbit *Sylvilagus floridanus* jack rabbit *Lepus sp* snowshoe hare *Lepus bairdi* Rabbits are the most prolific source of infection, being responsible for over 90 per cent of human cases in the United States with only 0 3 per cent of the cases occurring beyond the range of *Sylvilagus* sp (25) Persons who dress rabbits with bare hands are most likely to contract the disease such as market men hunters and housewives The organism may enter through a wound or cut or abrasion or directly through the unbroken skin No human case has been traced to domestic rabbits

Ticks Wood tick *Dermacentor andersoni* Dog tick *Dermacentor variabilis* Ticks bite under the skin or in the hair The wood tick has caused many cases in Montana and surrounding states while the dog tick is responsible for the disease in the southern and eastern states An outbreak of 50 cases among soldiers in Tennessee was attributed to the lone star tick, *Amblyomma americanum* (26)

Flies Deer fly *Chrysops discalis* The deer fly is the principal source of infection in Utah It bites on exposed parts of the body An outbreak of 30 cases was reported among 170 members of a camp of the Civilian Conservation Corps who worked stripped to the waist because of the heat The bare backs of the men offered an opportunity for the flies most of the lesions being on the back (14)

Other Insect Bites Insects of undetermined species have caused several cases (Thjotta reported a case apparently from a mosquito bite)

Animal Bites Tularemia has followed bites from the following animals cat kitten skunk coyote tree squirrel Montana ground

squirrel opossum dog hog lamb and white rat It is assumed that the mouth parts of the animal had been contaminated by feeding on infected material

Laboratory Infections Laboratory workers have been infected in many instances Infection was caused by the organism penetrating the skin of the hands or the conjunctiva

Ingestion Many cases in the United States have followed the ingestion of partially cooked rabbit meat Among 20 cases in 5 families there were 12 deaths In Russia in 1935 there was an epidemic of 43 cases among peasants who drank water from a brook thought to have been contaminated by water rats (13) Streams in the United States have been found contaminated with *P tularensis* (20)

Rats Water rat *Arvicola amphibius* Water rats caused more than a thousand cases in Russia in 1928 among persons who skinned the animals for their pelts Wild rats in Los Angeles and field mice in other parts of California have been found naturally infected but no human cases have been traced to them

Squirrels Tree squirrels have caused quite a number of cases among persons who dressed the animals California ground squirrels and the ground squirrels in Utah and Montana are infected but have caused no human cases

Sheep Sheep are not highly susceptible to tularemia Gwatkin (23) however reported an epidemic in Canada in which 25 sheep died The sheep herder was infected when skinning carcasses Sheepshearers in northwestern United States have been infected apparently by wood ticks in the wool

Opossum Several cases are reported among persons who had killed and skinned opossums

Birds A few human cases of tularemia have been reported following contact with pheasants and sage hens (27) Tularemia infection has been demonstrated in sharp tailed grouse and ruffed grouse in Minnesota and those birds are potential sources of danger

Miscellaneous Animals Human cases have followed contact with the following animals coyote deer red fox bull snake quail ground hog muskrat pig dog and skunk In many instances the victim of the disease had skinned or dressed the animal Several human cases followed the scratch of the cat the infection apparently being on the claws from contact with an infected animal

Eye Infections A considerable number of eye infections have

been reported the organisms being transferred to the eye by the hands while the person was dressing rabbits or after crushing flies or ticks Several cases resulted from infected material squirting into the eye from the animal being dressed

Potential Sources of Human Infection There are several potential sources of infection in the United States from which no human cases have been reported but which are dangerous Tularemia organisms have been isolated from the following animals in nature California ground squirrel ground squirrels in Utah and Montana field mice of California wild rats of Los Angeles gray foxes of Minnesota and the prairie dog in Utah The tick *Dermacentor occidentalis* in California and the rabbit flea in Minnesota are vectors of infection and potential sources of danger

THE DISEASE IN MAN

The incubation period of tularemia is about three days varying from one day to nine days The onset is sudden often occurring while the patient is at work There is headache chilliness vomiting fever and aches and pains in various parts of the body The sore at the site of the initial lesion develops while the associated lymph glands become enlarged and tender The duration of the disease is about three weeks with sweating loss of weight and much debility Convalescence is slow covering a period of two or three months Cases without complications recover with no bad after effects and with complete immunity against a second attack Foshay (16) reported a case that was apparently recovered but which developed a local lesion several months later from which tularemia organisms could be cultivated He drew attention to the danger of tularemia infection to hearts with preexisting vascular disease Tularemic pneumonia is being reported more and more often and is a serious disease (17) The tularemia organism is present in the sputum not only of persons with pneumonic lesions but also of those suffering from other types of the disease (24)

Several clinical types of tularemia have been reported

1 Ulceroglandular the primary lesion being a papule later an ulcer of the skin and accompanied by enlargement of the regional lymph glands

2 Oculoglandular the primary lesion being a conjunctivitis and accompanied by enlargement of the regional lymph glands Fulmi

nant cases running a rapid course with death have been noted in the oculoglandular type

3 Glandular without primary lesion but with enlargement of the regional lymph glands

4 Typhoidal without primary lesion and without glandular enlargements



FIG 54—Ulcer of right finger with axillary abscess in case of tularemia

5 Pneumonic usually without primary lesion and without glandular enlargements

6 Meningitic a rather rare occurrence (22)

Diagnosis of tularemia can be confirmed by several methods The organism may be cultivated from the lesion during the first two weeks of the disease either directly upon an appropriate culture medium or by guinea pig inoculation The skin test with the Foshay antigen of dead organisms may be positive as early as the third day of the disease it will also show a positive reaction when applied five years after recovery The agglutination test is positive in a high titer after a period of two weeks and remains so for many years

The mortality in 15 525 cases reported in the United States up to 1942 was 6 9 per cent

Foshay's serum produced by immunizing horses or goats with the tularemia organism has reduced the duration of the disease including the disability by about one half and the mortality by about one third in 240 cases

Penicillin is without effect in the treatment of the disease but streptomycin has given better results (27)



FIG 55—Tularemia due to tick bite

PREVENTION

Man can protect himself by avoiding contact with infected animals Laboratory workers should wear rubber gloves and take all possible precautions known to medical science Hunters market men and cooks should wear rubber gloves while skinning and dressing rabbits The hands should be thoroughly washed with soap and water after handling rabbits even though only the fur is touched Scratches and abrasions on the hands should be treated with a disinfectant

Thorough cooking destroys infection thus rendering a rabbit safe for eating purposes even though it may have harbored the disease Foshay has recommended the immunization of laboratory workers and persons engaged in the wild rabbit industry with a detoxified vaccine A considerable degree of protection is given but there are certain disadvantages which interfere with its general use Persons who have passed through a course of the disease are immune and may engage in such pursuits without danger

Isolation and quarantine of human cases and subsequent house disinfection are not necessary since there is no record of transmission of tularemia from person to person

An ordinance prohibiting the sale of wild rabbits has been used in some cities to reduce the morbidity and mortality of the disease during the rabbit hunting season

ITEMS OF NOTE

1 Tularemia is primarily a disease of rabbits although many other animals may be infected and act as hosts
2 About ninety per cent of human cases are acquired from rabbits
3 Domestic rabbits have never been known to acquire the disease naturally although they are entirely susceptible
4 There are a variety of arthropods which may act as vectors of infection
5 The virulance of *Pasteurella tularensis* is attenuated by residence in birds
6 The disease is rather widespread over the world

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CHAPTER XXI

LEPTOSPIROSIS

LEPTOSPIROSIS is an acute atypical or latent infection caused by the spirochete *Leptospira icterohemorrhagiae* or related species. Primarily it is an affection of rats and dogs; secondarily a disease of man. Other names by which the infection has been designated are Weil's disease, leptospirosis icterohemorrhagiae, spirochetosis icterohemorrhagiae, acute hemorrhagic jaundice, spirochetal jaundice, infectious jaundice and canicola fever. There are many cases of infectious jaundice which are not of spirochetal origin.

HISTORY

Infectious jaundice has been known to occur for many years among soldiers, sewer workers, ditch diggers, fishermen and persons subjected to water accidents. In the War of 1812 there were numerous cases among the soldiers, while in the American Civil War there occurred among the Northern troops more than 71,000 cases. The mild form of the disease together with the lack of fatalities would indicate that these outbreaks were not of spirochetal origin but rather an epidemic catarrhal jaundice due to a filtrable virus. Blumer (1) has reported many such outbreaks in North America.

Under the heading infectious jaundice in the past a large group of conditions have been included, from which from time to time have been separated such jaundices as those connected with malaria, yellow fever, typhoid fever, relapsing fever and the like. Leptospirosis has more recently been separated as a distinct entity.

Weil in 1886 reported four cases of disease in Europe in which there was a sudden onset of fever, chills, prostration and jaundice. Stimson in 1905 described a spirochete in the organs of a patient who had died in New Orleans presumably of yellow fever. He called the

organism *Spirochaeta interrogans*, it is now considered by most workers that it was *Leptospira*

In 1914 Inada and Ido in Japan transmitted to guinea pigs a disease similar to Weil s disease in Europe They discovered in human specimens as well as in the blood and organs of the guinea pigs an organism which they named *Spirochета icterohemorrhagiae* (2) It was not long before these results were confirmed in the armies of both the Allies and the Central Powers in the First World War The German investigators Hubener and Reiter (3) gave to the name of the organism isolated by them *Spirocheta nodosa* Noguchi (4) after making a comparative study of the spirochetes isolated in America, Europe and Japan proposed a new genus *Leptospira*

Meyer and his associates in 1939 called attention to leptospirosis in dogs

GEOGRAPHIC DISTRIBUTION

The distribution of leptospirosis is almost universal The spirochetes have been found in rats and dogs and demonstrated in patients in an increasing number of instances in all parts of the world

SEASONAL INCIDENCE

Leptospirosis occurs the year around but the majority of cases are reported during the summer months of June July August and September This coincides with the period of year when water infections are more apt to occur

THE ETIOLOGIC AGENTS

Leptospira icterohemorrhagiae is the responsible agent of the infection in rats *Leptospira canicola* which has been found in dogs is closely related and can be differentiated only by serologic means

Leptospira icterohemorrhagiae is a spiral organism with irregular wavy undulations with one or both ends sharply hooked when seen in free space In semi solid media the organisms appear bent waved or serpentine They are cylindrical in shape about 0 25 to 0 3 microns by 7 to 14 microns with sometimes long forms 30 to 40 microns The ends are usually drawn out into fine points although when resting they may appear blunt The motility is very rapid with a cork screw or serpentine movement along the whole length of the organism There is no flagellum however

The spirochetes are easily demonstrated in freshly drawn blood of infected guinea pigs by dark field illumination but are very difficult to find in blood from human cases Coagulation fibrils in fresh blood may be very misleading During the first four days of illness the diagnosis may be made more certain by concentrating the organisms by means of the centrifuge the spirochetes being found in the plasma sediment The method often fails because the spirochetes are not easily precipitated

Inoculation of guinea pigs with suspected human blood may be made during the first few days of infection but without certain success Some strains of leptospira exhibit a low pathogenicity even for young guinea pigs Packchanian has used deer mice with better results

The cultivation of leptospira may be carried out with material from sedimented blood specimens

Serologic tests have been found very satisfactory The Schuffner technic calls for an antigen either living or dead prepared from cultures grown on Verwoort s medium Agglutination tests carried out with living cultures are accompanied by the disadvantage of lysis of the spirochetes in the lower dilutions making readings impossible There is likewise an element of danger to the laboratory worker with living cultures

Agglutination tests carried out with an antigen of organisms killed with formalin have the advantage of being safer to the operator simpler to read no lysis in low dilutions and the possibility of absorption tests Care must be taken to use several strains of leptospira and to regard readings in titres under 1 300 without diagnostic significance

Leptospira hebdomadis is the cause of seven day fever in Japan The spirochete is similar to *L icterohaemorrhagiae* It finds its habitat in the field mouse *Microtus montebelli*

MODES OF TRANSMISSION

The manner in which man becomes infected with leptospirosis is given by Schuffner in the following order (57)

First the occupational hazard whereby fishermen bargemen slaughterhouse workers and others who work in localities infested by rats are exposed to infection Meyer (59) has called attention to the occupational hazard of veterinarians and others who work in dog pounds (canicola fever)

Second the water accident group consisting of persons who have fallen into and have been exposed for a considerable period of time to water polluted by human or animal refuse Similar water accidents in clean bodies of water do not result in infection

Third bathers and swimmers who are careless about the places which they frequent the water of which may be polluted

Numerous miscellaneous and sporadic cases occur from a variety of causes due to a known or unknown contact with an infected rat the presence of an infected dog in the home and similar occurrences

Passage of the spirochete through the unbroken skin probably does not take place but passage through the mucous membrane is possible which accounts for the water accident and bathing cases with penetration of the nasal or buccal membranes

Passage of the organism through wounds and abrasions must occur sometimes The possibility has been demonstrated by laboratory infections as well as by rat bite ferret bite and dog bite Another case of infection is reported when the victim with an abraded foot trod in the blood of a rat which had just been killed

In England an outbreak of 18 cases among coal miners was reported by Gulland and Buchanan (10) One out of every three rats examined showed infection Further study by Buchanan (29) however revealed that the habitat of the organism was in the roof slime of the coal mine The slime produced by the glutinous envelope of the organisms formed a jelly like or zoogleal mass In this the spirochetes multiplied in great numbers symbiotically with other organisms

ANIMAL INFECTIONS

Rats are apparently not at all inconvenienced by *Leptospira icterohemorrhagiae* The spirochetes are found in large numbers in the kidneys and are excreted in the urine They are present in the liver and other organs and may be excreted in the feces

Studies in various parts of the world have indicated that about 10 per cent of rats harbor the organism except in adult sewer rats where the rate is as high as 45 per cent (table 39)

Probably all rats are susceptible to infection the rate of infection depending upon various factors The sewer rat *Rattus norvegicus* is especially prone to harbor the spirochetes but the black rat *Rattus rattus rattus* and the roof rat *Rattus rattus alexandrinus* may

Table 39—PER CENT OF RATS INFECTED IN DIFFERENT LOCALITIES

PLACE	YEAR	INVESTIGATOR	RATS FOUND INFECTED
			Per cent
England	1918	Coles (8)	9
London	1919	Foulerton (9)	4
London	1922	Stevenson (61)	30
Aldershot England	1936	Coppinger (35)	43
Liverpool	1938	Mason (60)	33
Dublin	1931	O Connor (36)	40
Aberdeen Scotland	1934	Davidson and Smith (37)	24
Amsterdam	1922	Schuffner (57)	28
Rotterdam	1934	Schuffner (57)	25
Stockholm Sweden	1934	Olin (38)	6
Hamburg Germany	1934	Reiter (39)	14
Rome Italy	1935	Marchesi (40)	4
Belgium (war trenches)	1917	Stokes *et al* (7)	40
Brisbane Australia	1936	Johnson *et al* (41)	6
Brisbane Australia	1937	Johnson *et al* (41)	2
Queensland Australia	1934	Cotter *et al* (42)	30
Manila Philippines	1928	McKinley (43)	1
Japan (coal mines)	1917	Ido *et al* (6)	40
Guayaquil Ecuador	1934	Carbo-Noboa (44)	2
New York	1917	Noguchi (4)	17 2 to 21 9
Nashville	1917	Jobling and Eggstein (13)	10
Chicago	1919	Otteraaen (17)	3 to 52
Albany	192	Wadsworth (14)	40
Baltimore	1924	Robinson (15)	7
Washington D C	1924	Neill (16)	10
San Francisco	1931	Ridlon (45)	33
Rochester	1937	Syverton Berry (50)	38
Detroit	1937	Kasper (50)	16

carry the organisms though not in great numbers Old rats are infected to a much greater degree than young rats (table 40) The density of rat population is a factor according to Schuffner the rate of infection increasing with density of rat population Likewise epidemics among rats may be localized the rate of infection in one locality being as high as 56 per cent and in a nearby area as low as 11 per cent (57)

Infection passes from rat to rat by way of food which is polluted with infected urine and perhaps by sexual intercourse

Table 40—LEPTOSPIRA INFECTION IN SEWER RATS IN HOLLAND (57)

	TOTAL RATS EXAMINED	ADULT RATS POSITIVE PER CENT	YOUNG RATS POSITIVE PER CENT
Amsterdam 1923	207	45	2 5
1924	182	28	4
1925	401	17	3
1934	38	12	0
Rotterdam 1934			
Waterworks	30	11	0
Slaughter houses tables swimming baths	30	59	0

Second the water accident group consisting of persons who have fallen into and have been exposed for a considerable period of time to water polluted by human or animal refuse Similar water accidents in clean bodies of water do not result in infection

Third bathers and swimmers who are careless about the places which they frequent the water of which may be polluted

Numerous miscellaneous and sporadic cases occur from a variety of causes due to a known or unknown contact with an infected rat the presence of an infected dog in the home and similar occurrences

Passage of the spirochete through the unbroken skin probably does not take place but passage through the mucous membrane is possible which accounts for the water accident and bathing cases with penetration of the nasal or buccal membranes

Passage of the organism through wounds and abrasions must occur sometimes The possibility has been demonstrated by laboratory infections as well as by rat bite ferret bite and dog bite Another case of infection is reported when the victim with an abraded foot trod in the blood of a rat which had just been killed

In England an outbreak of 18 cases among coal miners was reported by Gulland and Buchanan (10) One out of every three rats examined showed infection Further study by Buchanan (29) however revealed that the habitat of the organism was in the roof slime of the coal mine The slime produced by the glutinous envelope of the organisms formed a jelly like or zoogleal mass In this the spirochetes multiplied in great numbers symbiotically with other organisms

ANIMAL INFECTIONS

Rats are apparently not at all inconvenienced by *Leptospira icterohemorrhagiae* The spirochetes are found in large numbers in the kidneys and are excreted in the urine They are present in the liver and other organs and may be excreted in the feces

Studies in various parts of the world have indicated that about 10 per cent of rats harbor the organism except in adult sewer rats where the rate is as high as 45 per cent (table 39)

Probably all rats are susceptible to infection the rate of infection depending upon various factors The sewer rat *Rattus norvegicus* is especially prone to harbor the spirochetes but the black rat *Rattus rattus rattus* and the roof rat *Rattus rattus alexandrinus* may

In California Meyer and his associates isolated 11 cultures of the canicola strain from dogs (59)

Raven (69) made agglutination lysis tests on 105 dogs in rural Pennsylvania finding 38 per cent positive to one or the other strain of the organism tests on fifty dogs in Philadelphia showed twenty eight per cent positive reactions The incidence of the infection increases with the age of the dog old dogs showing a higher rate than young dogs (table 41)

Table 41 —LEPTOSPIROSIS IN DOGS (RAVEN)

	NUMBER EXAMINED	PER CENT POSITIVE
Netherlands	212	39 6
Belgium	100	44 0
Germany	2[illegible]0	8 6
Italy (Rome)	112	3 6
United States		
New York	111	11 7
Santa Rosa	28	14 3
San Francisco	47	34 0
Pennsylvania (rural)	105	38 1
Philadelphia (urban)	0	28 0

Dogs may exhibit a marked jaundice The kidney is infected resulting in an acute or subacute and fatal infection Atypical and abortive cases occur the dogs which recover being carriers of the spirochete for several months and shedding them in the urine Klarenbeek in Holland found the dog strain (*L canicola*) less virulent for dogs than the rat strain The Holland cases were not complicated by icterus as were the cases reported by Meyer in California

Dogs may become infected possibly by eating infected rats They without doubt infect each other because of their interest in the urine of their own species Sexual intercourse may be a factor also

THE DISEASE IN MAN

Leptospirosis in man is initiated by alarming symptoms which appear quite suddenly consisting of distressing muscular pains a heavily coated tongue leucocytosis albuminuria meningeal symptoms and flushed conjunctivae During this febril period which lasts till about the fifth day spirochetes are present in the blood stream The icteric stage extends from the sixth to the thirteenth day when the fever decreases but hemorrhages may appear This is the fatal period The convalescent period begins at the fifteenth day and lasts to recovery Jaundice appears in about one third of the cases

Mice are subject to infection the house mouse *Mus musculus* as well as certain species of field mice being natural carriers

Packchanian (50) recommends five species as the most suitable for experimental studies—*Peromyscus californicus californicus P eremicus eremicus P maniculatus gambelli* (albino) *P polionotus polionotus* and *P truei truei*

Guinea pigs show resistance to some strains of leptospira Syverton studied over 800 guinea pigs infected with 34 strains strains of low virulence produced jaundice in only one per cent of the animals fever occurred in 80 per cent hemorrhages are generalized in only a few animals being confined to the lungs in 80 per cent of the cases

Rabbits are susceptible to infection, but are not ordinarily used as laboratory animals Other animals which may be experimentally infected include the gopher (Richardson ground squirrel) the weasel and the hamster

Foxes suffer from canine Weil s disease Dunkin and Laidlow (46) reported the presence of *L icterohemorrhagiae* in a fox found dead in a field Alston and Brown (47) mention three foxes that died of a similar infection on a fox farm Macrae (48) reports an outbreak in silver fox cubs where the organisms were demonstrated

Hogs have been reported on one occasion as responsible for a human infection Their relation to the disease lacks confirmation (48)

Horses may be infected experimentally but recover and display an immunity in the serum They do not apparently continue to harbor the organisms after recovery (49)

Cats may be infected sometimes Greene (64) made agglutination tests on 100 cats in California finding all of them negative for *L canicola* There was one positive reaction with *L icterohaemorrhagiae*

Dogs have assumed an increasingly important place in the epidemiology of leptospirosis They are infected with two strains of the organism *Leptospira icterhemorrhagiae* which is found in rats and *Leptospira canicola* which is never found in rats Klarenbeek in 1937 reported 21 dogs showing infection to the former and 31 dogs to the latter organism Borg Petersen and Jacobsen in Denmark found only one dog in 53 reacted to *L canicola* while 18 reacted to *L icterohemorrhagiae* Meyer examined 111 dogs in New York State 10 being infected with canicola and 3 with icterohemorrhagiae

Tabl ,⁰ —Distribution of Seventy three Cases of Lepto pirosis in the United States and Canada (Stiles and Sawyer)

10 swimmers
8 ewer workers
6 fish cutters
6 laborers
4 dairy workers
4 poultry dressers
4 who lived in cheap lodging houses
3 abattoir workers
2 laboratory workers
2 veterinarians
2 eating place operators
1 hoseman on a fire boat
1 golfer who waded in a river
1 who had a boil on his forearm which broke while he was searching for a golf ball in dirty stagnant water
1 butcher
1 who worked and slept in a rat infested kitchen
1 salesman in a meat and vegetable market
1 renovator in an old de erted carpet factory
1 quarry worker
1 machinist in a paper mill whose wife first had the infection
1 garage mechanic
1 unemployed brick mason
1 who moved wet lumber and waded in a river
1 who lived in a rat infested home and frequently trapped rats
1 who lived on a city dump for 18 years
1 rat catcher
1 who waded in a sewer creek
1 kitchen worker
1 worker on the construction of a gas main
1 schoolgirl
1 housewife
2 occupations not known

cupations three of which gave positive agglutination reactions for *L icterohaemorrhagiae* All tests for *L canicola* were negative Among the negative reactors were seventeen persons employed in handling dogs and nineteen men in the sewer maintenance department

Swan and McKeon (63) made agglutination tests on blood specimens of 101 coal miners in England finding only two that gave positive reactions both of whom gave definite histories of infection Subclinical infection did not exist at least in this group of coal miners

Laboratory workers have been infected on several occasions Five instances have been reported by Zeulzer in France and Germany two by Adamski in Warsaw (20) one by Alston and Brown in London (47) and two in the United States (67)

Mortality in the American group of cases was seventeen per cent for persons less than forty years of age and sixty three per cent for persons more than forty years (67) This is somewhat higher than the Netherland figures which were seven per cent for persons under

The total number of proved cases of leptospirosis in man in the United States up to 1937 was thirty two as reported by Packchanian (62) This was increased to sixty by Stiles and Sawyer (67) in 1940 Since that time additional reports from different parts of the country would indicate that many more cases exist Senekjie (66) found thirty cases in New Orleans in the five year period 1939 1944 In Cincinnati there were eight cases in one year (68) It would appear that better laboratory facilities for diagnosis has increased materially the number of cases reported

In other countries the number of cases reported has been larger In France in the period 1924 1932 there were 263 proved cases In Great Britain 1922 1939 there were 249 cases The Netherlands had 852 cases between 1924 and 1938 In Puerto Rico Larson reported 98 cases up to 1941

The majority of cases show evidence of infection with *L icterohaemorrhagiae* A small but increasing number of cases are infected with *L canicola* however

Leptospirosis is a disease of adults More males than females are infected probably because of occupational hazards The rather rare infections in children are difficult to explain because opportunity for infection must exist

Certain occupations expose workers to a risk of infection with leptospirosis Stiles and Sawyer (67) have drawn attention to the fact that courts in England Germany and the United States have awarded compensation to workers because of industrial infection The disease should be considered an occupational hazard rather than an occupational disease

In Great Britain among 142 cases occurring in a period of four years 99 were associated with fish workers coal miners and sewer workers Fifteen other cases followed bathing in rivers and canals (47) In Holland among 325 cases of known origin 68 were occupational including fisherman and others working in water or slaughter house workers and others working in places infested with rats The remainder of the cases followed swimming or water accidents In Australia in one year 138 cases were reported among sugar cane workers

In the United States among 73 cases tabulated by Stiles and Sawyer (67) there were eight sewer workers six fish cutters and a miscellaneous group of other occupations (table 42)

Greene (64) tested 426 blood serums from persons of various oc

Table 4[a] —Distribution of Seventy three Cases of Leptospirosis in the United States and Canada (Stiles and Sawyer)

10 swimmer
8 sewer workers
6 fish cutters
6 laborers
4 dairy workers
4 poultry dressers
4 who lived in cheap lodging houses
3 abattoir workers
2 laboratory workers
2 veterinarians
2 eating place operators
1 hoseman on a fire boat
1 golfer who waded in a river
1 who had a boil on his forearm which broke while he was searching for a golf ball in dirty stagnant water
1 butcher
1 who worked and slept in a rat infested kitchen
1 salesman in a meat and vegetable market
1 renovator in an old deserted carpet factory
1 quarry worker
1 machinist in a paper mill whose wife first had the infection
1 garage mechanic
1 unemployed brick mason
1 who moved wet lumber and waded in a river
1 who lived in a rat infested home and frequently trapped rats
1 who lived on a city dump for 18 years
1 rat catcher
1 who waded in a sewer creek
1 kitchen worker
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1 schoolgirl
1 housewife
2 occupations not known

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forty years and thirty three per cent mortality for persons over forty years

PREVENTION

The prevention of spirochetal jaundice is a sanitary measure Those persons engaged in occupations where infection is likely to take place should take special precautions Ditch workers and sewer workers should protect themselves by boots and shoes Fish workers should take all sanitary precautions as well as to prevent the entrance of rats into the establishments The extermination of rats has been emphasized as an important prophylactic measure The urine of infected dogs should be avoided Active immunization with a vaccine which affords protection for a period of six to twelve months has been used but is not considered practical

An immune serum has been prepared using either horses or goats Favorable results have been obtained with such serums when administered before the appearance of jaundice

Convalescent human serum has been used to some extent

ITEMS OF NOTE

1 Leptospirosis is caused by a *Leptospira icterohemorrhagiae* or the closely associated spirochete *Leptospira canicola*
2 The natural habitat of *L icterohemorrhagiae* is the rat or the dog
3 The habitat of *L canicola* seems to be the dog
4 The disease prevails in almost all portions of the world
5 Prevention consists in sanitary precautions

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forty years and thirty three per cent mortality for persons over forty years

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CHAPTER XXII

RAT BITE FEVER

RAT BITE fever is primarily an affection of rats secondarily man is infected following the bite of a rat or sometimes of a weasel ferret squirrel or cat

The term sodoku is common for the disease in Japan and is found in English and American literature

HISTORY

Rat bite fever is said to have existed in the fourth century B C in India from whence it spread to the rest of the world

In the United States it has been known for more than a century cases having occurred in 1830 according to Blumer (20) Carter in 1887 observed an organism in the blood of a naturally infected rat in India to which he applied the term *Spirillum minus* In 1900 Miyake (1) brought the disease to the attention of European investigators who up to that time had quite ignored it only two cases having appeared in European literature In 1916 Futaki (14) and his associates in Japan described the causative agent of the disease which they called *Spirocheta morsus muris*

PREVALENCE AND DISTRIBUTION

Rat bite fever is of world wide distribution In England the first cases were reported by Horder in 1909 since which time the disease seems to have become quite prevalent In France Spain Italy Germany and other European continental countries reports have been received from time to time In 1915 Crohn (12) collected histories on 24 Japanese cases 16 American 8 English 2 French 1 Italian and 1 Indian The next year Blake (13) added 28 more histories making 81 During the ten years from 1918 to 1927 there were reported 90 cases from nineteen different countries Ruge in 1929 reviewed 329 cases that had been reported up to then occurring in many parts of the world In India during a nine year period

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Spirillum minus has been found in the wound at the site of the bite in the lymph and salivary glands and in the circulating blood There are numerous failures however in attempts to demonstrate its presence in patients It cannot be cultivated on any artificial culture media and is difficult or impossible to demonstrate by dark field technic with blood or lymph from the patient The best method is animal injection either guinea pigs or white mice using blood or lymph aspirated from the lesion A piece of tissue removed from the lesion may also be inserted under the skin of the test animal with good results After about two weeks the spirochetes may be demonstrated in the blood by darkfield or in stained films

Streptobacillus moniliformis is the cause of Haverhill fever The organism is transmitted by the bite of the rat and is sometimes confused with *Spirillum minus*

THE DISEASE IN ANIMALS

Infection of rats with *Spirillum minus* does not seem to inconvenience them The Japanese workers (14) did not find the organism present in the blood of all rats and there was no relation between the kind of rat and the ratio of infection They found the organism only in the blood stream and not in the saliva and it was suggested that possibly transmission of the spirochete from rat to man occurs from infection of the wound through bleeding gums Later investigation however showed the spirochetes present in the saliva and it is undoubted that the spirochete is conveyed in this way About 3 per cent of brown rats have been found infected Leadingham (15) found 73 rats in Atlanta Georgia to be free of infection Bayne Jones could find no spirochetes in the rats of Rochester N Y In Amsterdam one per cent of rats were reported to be infected while in London 25 per cent were found infected

Field mice in Germany and the United States have caused human infections (32) In India 48 per cent of white mice were found to be naturally infected with S *minus*

Arima (23) has reported that white rats are more resistant to Manila strains of the spirochete than are white mice and both are much more resistant than are guinea pigs rabbits and Philippine monkeys for which that organism is very virulent

Transmission of rat bite fever occurs directly from rat to rat because rats eat other rats dead from whatever cause some of which may harbor *Spirillum minus* Arima could not find that fleas are a

70 cases were diagnosed at the Calcutta School of Tropical Medicine by demonstration of the spirochete (28) Swarup believes however that this constitutes a very small number of cases compared to the rat population of India In Canada in 1933 Stewart (24) reported 7 cases six of which were in Montreal Newfoundland had none Mexico in ten years time (1918 27) reported but one case indicating that most of that country is free from infection Cuba and Central America are said to have had no cases reported (16) In the United States Wilcox (2) in 1839 reported a case in a man forty years old The next year Watson (3) gave an account of a seaman bitten by a rat over the eyebrow, who developed the disease In 1869 there was a mother and son reported by Gilliam (4) who developed the disease within two days of each other Three reports appeared in 1872 by Packard (5) in Philadelphia and Earle (6) and Reece (7) in Chicago Cook (8) in 1855 had one case and Banker (9) in 1886 four cases In 1901 Evans (10) published an account of three cases Two girls were bitten by the same rat at the same time both of whom took sick on the same day three weeks later Proescher (11) in 1912 added another

Bayne Jones (21) in 1931 found 81 cases that had occurred in the United States over a period of ninety years Wooley (35) increased the figure to a total of 110 in the next 10 years scattered over 28 states The only large area from which no cases were reported was the sparsely populated Rocky Mountain region

Additional cases of rat bite fever have been reported since then but the total number that have occurred is not known Richter (34) reports 93 persons bitten by rats in a four year period in Baltimore 65 of whom came from an area of two square miles There were 7 cases of rat bite fever In the same period there were probably many more persons bitten by rats who went to private physicians or who treated the bites themselves Richter believes that rats develop a taste for human blood and after biting a person once they will return for a further meal If not driven away they will continue to eat a considerable portion of flesh Infants are the chief sufferers One child in Baltimore was bitten on eleven different nights

might wipe off the organism from the teeth The bite of an infected animal does not invariably result in infection since there are several instances of two persons being bitten by the same rat and only one contracting the disease

The mortality from rat bite fever is usually stated as about 10 per cent Bayne Jones (21) however after correcting the figures on 81 cases in the United States and removing such cases as did not be long in the list gave the mortality as 6 per cent From 1920 to the time he published his report (1930) no case died in the United States

PREVENTION AND CONTROL

The prevention of rat bite fever is accomplished by the various methods which have been devised for the suppression and destruction of rats Prophylactic treatment of persons who have been bitten consists in prompt cautery of the wound with antiseptic dressings The cure of the disease has been accomplished by the use of the arsenical drugs and by penicillin

ITEMS OF NOTE

1 Rat bite fever is caused by *Spirillum minus*
2 The spirochete causes no inconvenience in rats
3 Human cases have been reported in America for nearly a century
4 The disease in man is contracted by the bite of an infected rat rarely by other animals
5 The prevention of the disease consists in the elimination of rats

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factor in spreading the infection from rat to rat or from rat to man The spirochetes remained viable only a short time in the body of the flea and did not multiply there

Rat bite fever following the bite of a cat has been reported in several instances (16) while Nixon (17) describes the same condition following the bite of a ferret and Schottmuller (18) the bite of a squirrel The weasel has likewise been implicated by Dick and Tunnicliff (19) as has also the dog (25) Iver reported 2 cases from monkey bites (26) and Pillai a case from the bite of a bandicoot (27) The bite of a pig has caused human infections All such animals must be considered probably as mechanical carriers

THE DISEASE IN MAN

Rat bite fever in man is characterized by a local inflammatory condition about the site of the bite wound with enlargement of the contiguous lymphatic glands and accompanied by paroxysms of fever followed by periods of remission

Crohn (12) studied a large number of cases finding the incubation period to average twelve days The more severe the bite however the shorter the incubation period and the more severe the illness Cases in which the incubation period lasted from 1 to 5 days the illness endured 111 days incubation period 6 to 15 days illness 50 days incubation period 16 to 35 days illness 54 days

Occupation age and sex play no part in susceptibility to infection but are of some significance in the possibility of exposure Crohn reported 31 males to only 20 females Bloom (30) gives the figures for 70 cases in the United States as 37 males and 23 females Adults are often infected especially men and grown boys in such occupations as seamen and farmers Van der Bogert (31) could find only 6 cases under 2 years of age in the United States from 1921 to 1933 Other investigators have reported a considerable number of cases in infants Young children while sleeping are more apt to be bitten by rats than are adults Richter found that 60 per cent of persons bitten in Baltimore were under one year of age

The *location of the wound in the majority of cases is on an* extremity In 52 of Crohn s cases it was on the hand and arm 36 times face and head 11 leg and foot 3 and not noted 2 Swab (29) reports a child bitten through both the upper and lower lids of one eye As in rabies a bite on an exposed surface was more apt to result in infection than on a protected surface where the clothing

CHAPTER XXIII

HAVERHILL FEVER

(Erythema Arthriticum Epidemicum)

HAVERHILL Fever (erythema arthriticum epidemicum) is primarily an infection of rats Man contracts the disease directly by the bite of an infected rat or indirectly through milk

HISTORY

Haverhill fever was not recognized as a clinical entity until 1926 For some years before that time however there were cases reported as rat bite fever from which an organism different from *Spirocheta morsus muris* was isolated Schottmuller (1) in Germany was apparently the first to make such a report in 1914 In the next ten years Blake (2) Litterer (3) Dick (4) and Tunnicliff (5) in the United States encountered similar conditions Ebert and Hesse (6) in Russia Thorp (7) in England and Levaditi and his coworkers (8) in France published other reports

The milk epidemic at Haverhill Massachusetts in 1926 was studied in detail by Place Sutton and Willner (9) and served to focus attention on the disease The term erythema arthriticum epidemicum was used by these authors as the designation for the affliction Later in the same year Dodd (10) reported a case that had occurred in Baltimore in 1923 using the same name

Two sporadic cases in Boston were reported by Hazard and Goodkind (11) in 1932 and by Scharles and Seastone (12) in 1934 The causative organism was isolated in each instance In the second there was a history of rat bite but none in the first Other authenticated reports have been made with isolation of the organism Lemierre and his coworkers (13) in France described a case in a railway worker due to rat bite Farrell Lordi and Vogel (14) reviewed thirteen sporadic cases up to 1939 and added another from

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GEOGRAPHIC DISTRIBUTION

Haverhill fever is probably widespread although adequate reports are lacking Cases resembling the disease have been reported from Russia Germany France and England as well as from various parts of the United States Milk epidemics have occurred in Pennsylvania and Massachusetts while sporadic cases have been reported in Massachusetts Tennessee Illinois Maryland New York Virginia Oklahoma Michigan and Washington D C

THE ETIOLOGIC AGENT

Streptobacillus moniliformis (*Haverhillia multiformis* *Streptothrix muris ratti*) is a gram negative rod 2 to 5 microns in length and 0 1 to 0 4 microns in width It is pleomorphic however and under favorable conditions it may be observed in filaments 30 to 40 microns long It grows best in blood broth or ascitic fluid broth the growth appearing at the bottom of the tubes While the organism prefers partial anaerobiosis it is not an obligate anaerobe

The organism can be cultivated readily from the blood of patients during the first three weeks of the disease It is virulent for white mice but not for rabbits It will agglutinate patients serum taken during the second week after onset in dilutions up to 1 640 Allbritten Sheeley and Jeffers have suggested procedures for the identification of *Streptobacillus moniliformis* to distinguish it from *Spirillum minus* (table 43)

Parker and Hudson (22) placed the organism in the order *Actinomycetales* in the family *Mycobacteriaceae* and considered it a new genus *Haverhillia multiformis*

MILK EPIDEMICS

Two epidemics due to raw milk are on record The outbreak at Chester Pennsylvania in May and June 1925 was studied by Armstrong and Wood but was not reported at the time Place and Sutton (21) in making a final report on the Haverhill epidemic reviews the Chester incident because of the striking similarity of onset symptoms and course of disease and the epidemiologic relation to the milk supply There were about six hundred cases Ninety two per cent of the known patients received raw milk from a single bottling plant in the city while half of the remainder had partaken

Brooklyn Allbritten Sheely and Jeffers (15) described a case in Philadelphia in a laboratory worker bitten by a white rat In 1941 Kirkwood and Stoll (16) encountered a case in Illinois, Hart (17)

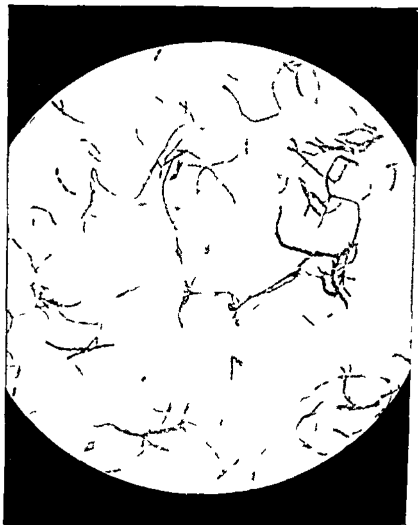


Fig 56 —*Streptobacillus moniliformis* cause of Haverhill fever
Courtesy of Dr F Parker Jr

reported a case in a college student in Virginia while Larson (18) described two cases in Washington D C In 1943 Ishmael reported a case due to rat bite the first to be recognized in Oklahoma Wheeler (24) reported 3 cases in Detroit in 1945

Tunnicliff (5) showed that the etiologic agent of the disease was carried by the rat as a benign inhabitant of the lung Strangeways (20) and Lemierre (13) both demonstrated the organisms in the nasopharynx of the rat The rat does not seem to be inconvenienced in any way

THE DISEASE IN MAN

The Haverhill milk epidemic was described by Place Sutton and Willner (9) as a disease characterized by an abrupt onset with chills fever malaise vomiting and headache an early eruption rubellaform or morbilliform occurring on the extremities and tending to become hemorrhagic a multiple arthritis of varying but often of a severe and crippling degree a fever curve of abrupt rise with remission in from two to five days and after a few days of relative freedom from symptoms a recurrence with which the arthritic manifestations appear

The disease due to rat bite does not differ in its clinical features from milk borne infection The wound usually heals promptly and shows little if any reaction

The incubation period usually is from two to ten days but sometimes longer In the milk epidemics it was short—often two or three days The time seems to be dependent upon the number of organisms causing the infection

Table 14—DIFFERENTIATION OF HAVERHILL FEVER FROM RAT BITE FEVER AFTER HART (17)

	HAVERHILL FEVER	RAT BITE FEVER
Infecting organism	Streptobacillus	Spirillum
Portal of entry	Animal bite Milk borne	Animal bite
Incubation period	Short 2 to 10 days	Long 10 to 20 or more days
Wound healing	Prompt as a rule	Induration and adjacent lymphadenitis
General symptoms	Prompt severe	Delayed less severe
Arthritis	Common	Rare
Rash	Morbilliform petechial	No petechial
Leukocytosis	Marked	Slight
Treatment	Penicillin	Arsenic penicillin

Contact infection from person to person does not seem to occur

The death rate is very low Blake (2) and Tunnicliff and Mayer (5) reported fatal cases There were no deaths in the Chester epidemic

There has been some confusion in the differentiation of Haverhill

of milk from the same source in restaurants The etiology of the disease was not determined

Table 43 —LABORATORY DIAGNOSIS OF STREPTOBACILLUS MONILIFORMIS AND SPIRILLUM MINUS INFECTIONS AFTER ALLBRITTEN SHEELEY AND JEFFERS (15)

PROCEDURE	SPIRILLUM MINUS	STREPTOBACILLUS MONILIFORMIS
Blood culture	No growth on ordinary mediums	Draw blood at height of fever add to beef bouillon characteristic growth in 24 to 28 hours ascitic fluid or serum enrichment of mediums needed for all subcultures
Animal inoculation	Inoculate mice and guinea pigs intraperitoneally with 2 cc of citrated blood or material aspirated from bite wound or adjacent enlarged lymph node daily dark field examination of inoculated animals blood for *Spirillum minus* if Spirillum minus is found before 5th day it is probably a natural infection	Inoculations with patient s tissue fluids give negative results inoculations of cultures into mice result in polyarthritis and death not pathogenic for rats and guinea pigs
Tissue fluid	Dark field examination of patient s blood serum from wound or involved lymph node (rarely positive) stained preparations of tissue fluids by Wright s Giemsa s or Fontana s stain (rarely positive)	Centrifuge joint fluids and examine smear take culture of joint fluid in ascitic or serum bouillon
Serologic reaction	Technically difficult and of questionable value	Positive agglutination precipitin and complement fixation may offer confirmatory evidence

The outbreak in Haverhill Massachusetts occurred in January 1926 Thirty nine families were involved with eighty six cases all living in a small area The age of the patients varied from two years to fifty four years The milk in every case came from a small dairy selling raw milk When the milk was pasteurized the epidemic stopped The etiologic agent was shown to be *Streptobacillus moniliformis* The source of contamination of the milk is not known but it is presumed that rats were involved

THE INFECTION IN RATS

The rat seems to be the principle animal reservoir of *Streptobacillus moniliformis* The only other animal implicated is the weasel reported by Dick and Tunnicliff (4) Mice injected with cultures of the organism develop polyarthritis and die Rabbits are refractory to the disease

Tunnicliff (5) showed that the etiologic agent of the disease was carried by the rat as a benign inhabitant of the lung Strangeways (20) and Lemierre (13) both demonstrated the organisms in the nasopharynx of the rat The rat does not seem to be inconvenienced in any way

THE DISEASE IN MAN

The Haverhill milk epidemic was described by Place Sutton and Willner (9) as a disease characterized by an abrupt onset with chills fever malaise vomiting and headache an early eruption rubellaform or morbilliform occurring on the extremities and tending to become hemorrhagic a multiple arthritis of varying but often of a severe and crippling degree a fever curve of abrupt rise with remission in from two to five days and after a few days of relative freedom from symptoms a recurrence with which the arthritic manifestations appear

The disease due to rat bite does not differ in its clinical features from milk borne infection The wound usually heals promptly and shows little if any reaction

The incubation period usually is from two to ten days but sometimes longer In the milk epidemics it was short—often two or three days The time seems to be dependent upon the number of organisms causing the infection

Table 4 —DIFFERENTIATION OF HAVERHILL FEVER FROM RAT BITE FEVER AFTER HART (17)

	HAVERHILL FEVER	RAT BITE FEVER
Infecting organism	Streptobacillus	Spirillum
Portal of entry	Animal bite Milk borne	Animal bite
Incubation period	Short 2 to 10 day	Long 10 to 20 or more days
Wound healing	Prompt as a rule	Induration and adjacent lymphadenitis
General symptom	Prompt severe	Delayed less severe
Arthritis	Common	Rare
Rash	Morbilliform petechial	No petechial
Leukocytosis	Marked	Slight
Treatment	Penicillin	Arsenic penicillin

Contact infection from person to person does not seem to occur

The death rate is very low Blake (2) and Tunnicliff and Maver (5) reported fatal cases There were no deaths in the Chester epidemic

There has been some confusion in the differentiation of Haverhill

fever from rat bite fever when the disease was caused by the bite of a rat Hart (table 44) has assembled the salient points of distinction

PREVENTION AND CONTROL

The prevention of Haverhill fever depends on the control of rats Sporadic cases occur from rat bite while epidemics result from milk supplies contaminated apparently by rats Compulsory pasteurization of milk should be required as an added safeguard

Penicillin has been recommended in the treatment of the disease (23)

ITEMS OF NOTE

1 Haverhill fever is caused by *Streptobacillus moniliformis*
2 *The rat is the chief reservoir of infection*
3 Sporadic cases occur from the bite of infected rats
4 Epidemics arise from unpasteurized milk apparently infected by rats
5 The prevention of the disease consists in the elimination of rats

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CHAPTER XXIV

ENDEMIC RELAPSING FEVER

ENDEMIC relapsing is a disease caused by several closely related spirochetes Wild rodents and other animals are reservoirs of infection of the endemic type of the disease from which the spiro chetes are transmitted to man by ticks of the *Ornithodorus* variety (Epidemic relapsing fever is spread directly from person to person by the body louse)

HISTORY

Epidemic relapsing fever carried by the body louse has been wide spread over the world probably since the time of Hippocrates Several severe epidemics have occurred in the United States Obermeier in 1873 showed that the disease was caused by a spirochete Mackie in 1907 described an epidemic due to the body louse

Endemic relapsing fever in the United States was first reported by Meador (1) in Colorado in 1915 It was encountered in California in 1922 and in Texas in 1927 Weller and Graham (13) called attention to the tick as a vector in 1930, which marks the beginning of real interest in the disease in this country (16) Ross and Milne in 1904, and Dutton and Todd independently had already demonstrated that the tick could transmit the disease

SEASONAL PREVALENCE

Relapsing fever in the United States occurs mostly during June July and August (5) which represents the season when ticks have an opportunity to bite their victims In warmer countries tick borne relapsing fever prevails throughout the year

The louse borne form of the disease which occurs in Europe and Asia has its greatest prevalence in winter and spring

AGE AND SEX

Most cases of relapsing fever in the United States occur in males probably because of greater exposure and opportunity of infection

There is no indication that females are more resistant nor that age has any connection with immunity

DISTRIBUTION

Endemic relapsing fever has been encountered in various parts of Africa Asia and Europe In the western hemisphere it has occurred in Venezuela Peru Brazil Uruguay Argentina Panama Cuba Mexico and Canada

In the United States it has been reported from a dozen or more western states including Arizona California Colorado Idaho Kan sas Nevada New Mexico Oklahoma Texas Utah Washington and Wyoming In addition ticks of the *Ornithodorus* species have been found in Florida Minnesota Montana New York and Wisconsin

THE ETIOLOGIC AGENTS

Relapsing fever is caused by spirochetes of the genus *Borrelia* Several different members of this group have been described as be ing responsible Morphologically they are indistinguishable They are delicate organisms averaging about 17 microns in length (vary ing from 5 microns to 36 microns) with three to six spiral turns The ends are pointed In fresh blood specimens they exhibit a very active screw like movement Artificial cultivation can be carried out by the use of sterile ascitic fluid containing citrated blood and fresh kidney Incubation for seven days at 37 C under anaerobic con ditions is necessary The organisms can be stained by the Romanow sky or similar method

In many laboratories the spirochetes have been kept alive by in jecting a mouse or rat every third day Beck (6) showed that the organisms would remain alive in defibrinated sheep blood at re frigerator temperature for as long as 195 days Injection of mice was made every two months therefore instead of every two days It would seem that infected ticks might afford an even less laborious and a surer method of preserving the living spirochete

The nomenclature of this group of spirochetes is confusing *Bor relia recurrentis* (*Spirocheta recurrentis Spirocheta obermeiri Tre ponema recurrentis*) was discovered by Obermeier It causes the epidemic type of relapsing fever spread by the body louse in Europe and elsewhere

There are several spirochetes that are transmitted by ticks which have been designated by different names according to the locality

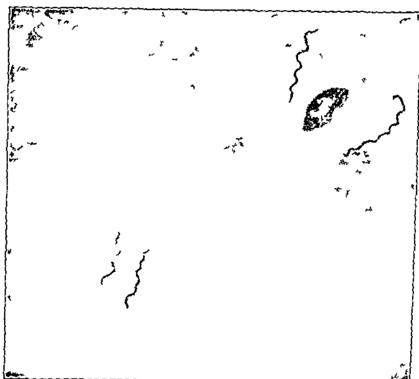


FIG 57 —*Borrelia recurrentis* Texas strain in blood of white mouse (A M M 50437)

in which they were found They may or may not be identical Thus *Borrelia duttoni* is found in Central Africa *Borrelia persia* in Persia and Northwest India *Borrelia hispanica* in Spain and Morocco and *Borrelia marocanus* in Morocco In the United States *Borrelia turicata* is associated with the tick *Ornithodorus turicata* *Borrelia parkeri* with *O parkeri* and *Borrelia hermsi* with *O hermsi* *Borrelia venezuelensis* (*neotropicalis*) is found in Venezuela Colombia and Panama *Borrelia novyi* (sometimes called the American strain) was isolated by Novy from an immigrant to the *United States* It has not been associated with endemic relapsing fever

It has been emphasized by various workers (6) that immunologic reactions are not entirely reliable in differentiating *these spirochetes* for the same organism may give different reactions when tested in different stages of relapse Differences in virulence may be the result of environment *over a period of time* *Even though all the* strains are but variants of *Borrelia recurrentis* the different designations should probably be maintained for purposes of convenience

MODES OF TRANSMISSION

The epidemic type of relapsing fever is transmitted from person to person by the body louse *Pediculus humanus*

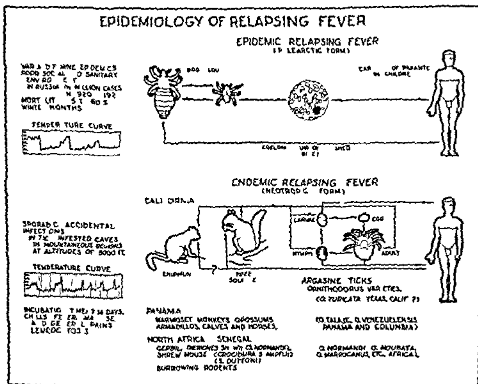


FIG 58 —Epidemiology of relapsing fever showing reservoirs of infection and methods by which the disease is transmitted (Meyer)

The endemic type is transmitted from animal to animal and from animal to man by the argasine tick genus *Ornithodorus* The argasine tick (family *Argasidae*) is characterized by the fact that when viewed from above only the legs are seen outside the body the head and mouth parts being concealed The genus *Ornithodorus* is distinguished from the other members of this family genus *Argas* by the rounded edge of the body There are numerous species of the genus *Ornithodorus* the species responsible for transmitting relapsing fever varying according to geographic location (table 45)

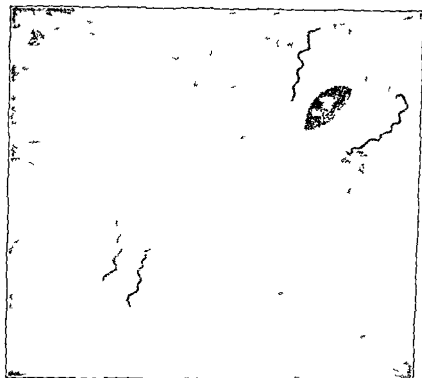


FIG 57 — *Borrelia recurrentis* Texas strain in blood of white mouse (A M M 50437)

in which they were found They may or may not be identical Thus *Borrelia duttoni* is found in Central Africa *Borrelia persia* in Persia and Northwest India *Borrelia hispanica* in Spain and Morocco and *Borrelia marocanus* in Morocco In the United States *Borrelia turicata* is associated with the tick *Ornithodorus turicata* *Borrelia parkeri* with *O parkeri* and *Borrelia hermsi* with *O hermsi* *Borrelia venezuelensis* (*neotropicalis*) is found in Venezuela Colombia and Panama *Borrelia novyi* (sometimes called the American strain) was isolated by Novy from an immigrant to the United States It has not been associated with endemic relapsing fever

It has been emphasized by various workers (6) that immunologic reactions are not entirely reliable in differentiating these spirochetes for the same organism may give different reactions when tested in different stages of relapse Differences in virulence may be the result of environment over a period of time Even though all the strains are but variants of *Borrelia recurrentis* the different designations should probably be maintained for purposes of convenience

ANIMALS SUSCEPTIBLE

A considerable number of animals act as hosts of endemic relapsing fever depending upon the locality In western United States there are a variety of rodents such as chipmunks ground squirrels prairie dogs kangaroo rats white footed mice and other burrowing rodents that have been found to harbor the spirochetes The red tree squirrel was also found infected in California In Texas the armadillo and opossum are reservoirs of infection (14)

In Panama opossums armadillos squirrel monkeys calves and horses are possible hosts In West Africa certain species of rats are infected while in North Africa the shrew is a host

Experimental infection has succeeded with monkeys guinea pigs white rats and white mice Rabbits seem to be poor hosts although infection sometimes does take place

THE DISEASE IN ANIMALS

The course of the disease in animals varies with the strain of spirochete and the animal Thus *Borrelia recurrentis* and *Borrelia persia* cause mild reactions while *Borrelia hispanica* *Borrelia duttoni* and *Borrelia venezuelensis* cause severe reactions

Monkeys and rodents generally speaking are susceptible to all types In white mice the incubation period is about three days with variations according to the size of the doses and the method of inoculation The animals become visibly sick with roughed fur and closed eyes This lasts for a period of two to five days during which time enormous numbers of spirochetes are present in the blood after which they disappear and the animal becomes apparently normal for several days Then there is a relapse and the process is repeated Usually there are two or three relapses

Some mice become paralyzed (neurotropic form of infection) living for two weeks or more before they die

Some rodents have an acquired immunity showing no symptoms although spirochetes are present in the blood

THE DISEASE IN MAN

The incubation period in man of endemic relapsing fever varies from six to nine days The onset of symptoms are usually sudden with high fever chills frontal headaches intense pains in the back limbs and joints together with varying other disturbances The

Adult ticks of the species *O turicata* were found by Francis to live five years without feeding and to harbor virulent spirochetes of relapsing fever throughout that time when fed they were alive and in good condition at the end of seven and one half years (15)

Table 45 —TICKS WHICH HARBOR SPIROCHETES OF RELAPSING FEVER IN DIFFERENT LOCALITIES

O turicata	Kansas New Mexico Oklahoma and Texas in the United State Mexico
O hermsi	California Colorado Oregon Washington Nevada Idaho and Briti h Columbia
O parkeri	California Idaho Montana Nevada and Wyoming
O rudis	(O venezuelen is) Panama Colombia and Venezuela
O talaje	Panama Colombia and Guatemala Arizona and Texas
O moubata	Central and East Africa
O tholozani	(O papillipes) Iraq Iran Indian Russian Turkestan and Palestine
O lahorensis	Iran India and Russian Turkestan
O erraticus	(O marocanus) Spain and Western North Africa
O savignyi	Egypt North and East Africa
O asperus	Iraq
O tartakovskyi	Russia
O verrucosus	Caucasus

Ticks are natural parasites of rodents but are not averse to feed ing upon other animals including the human The adult tick is large enough to be noticed and removed If it bites a person the lesion is of sufficient extent so that there is a definite history of a bite The nymphal forms are capable of transmitting the disease

The spirochetes are capable of penetrating the mucous membrane and sometimes even the unbroken skin as when the feces from an infected tick are rubbed into the skin

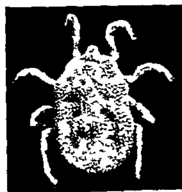


FIG 59 —Argasine tick *Ornithodorus turicata U S Dept Agriculture Bureau of Entomology and Plant Quarantine*

The manner in which ticks transmit the infection to a new host seems to vary In some instances the coxal fluid and feces carry the spirochetes which are deposited on the skin and enter through the wound caused by the bite or are rubbed into the skin Other experiments have shown that the spirochetes enter directly through the bite

The adult tick, once it has become infected remains so for life The spirochete is transmitted to the next generation with great regularity Davis (17) has suggested that the tick itself may be a more efficient spirochetal reservoir than the rodent host

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first attack lasts about three days when the temperature falls and the patient feels quite normal except for weakness After four or five days (the period varying according to the severity of the disease) a relapse occurs, with symptoms similar to the first attack but somewhat less severe Without treatment there are two to four or more relapses

Spirochetes are found in the blood during the febrile periods Chung (11) has shown that they likewise appear and disappear in the urine He has demonstrated them in the spinal fluid during the course of the disease (12) Diagnosis can be verified by the complement fixation test according to Stein (18), using an antigen of spirochetes, washed from the blood of infected rats or mice

The death rate in American cases has been very low Treatment by penicillin has been effective experimentally (19)

PREVENTION

The prevention of endemic relapsing fever is a matter of avoiding infected ticks Cottages and camp sites where infected rodents may nest should be thoroughly cleaned Adult ticks should be removed from the clothing when found Since the nymphs may escape discovery, they are probably more potent sources of danger than the adults

ITEMS OF NOTE

1 Endemic relapsing fever is transmitted by the tick *Ornithodorus* of which there are numerous species in different parts of the world
2 The etiologic agents are spirochetes of the genus *Borrelia*
3 The reservoir of infection is one or another of the rodents or other animal varying according to geographic location
4 The endemic infection in man in the United States is largely confined to rural and sparsely settled areas

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diseases are for typhus—fleas and lice for Rocky Mountain spotted fever—ticks for tsutsugamushi (scrub typhus)—mites There are several other diseases which belong to the Rickettsia group the relationship of which to the other members of the group as yet has not been definitely determined as trench fever boutonneuse fever Kenya typhus and certain South African tick fevers

Table 46 —RICKETTSIAL DISEASES TRANSMITTED FROM ANIMALS TO MAN

DISEASE	ETIOLOGIC AGENT	VECTOR	ANIMAL RESERVOIR
Murine typhus fever	*Rickettsia mooseri*	Rat flea *Xenopsylla cheopis*	Rat
Rocky Mountain spotted fever	*R rickettsi*	Wood tick *Dermacentor andersoni* Eastern dog tick *Dermacentor variabilis*	Rodents and other animals
Brazilian and Columbian spotted fevers	*R rickettsi*	Cayenne tick *Amblyomma cajennense*	Dog
Boutonneuse fever and Kenya typhus	*R conori*	Brown dog tick *Rhipicephalus sanguineus*	Dog
South African tick bite fever	*R pijperi*	*Haemaphysalis leachi*	Dog
Tsutsugamushi disease	*R orientalis*	Kedani mite *Trombicula akamushi*	Field rats and mice
Q fever	*R burneti*	Several ticks *Haemaphysalis humerosa* *Ixodes holocyclus* *Boophilus annulatus* *Dermacentor andersoni* *Amblyomma americanum*	Bandicoot rats cattle

The Rickettsiae of epidemic typhus have been named *Rickettsia prowazeki* and the rickettsia that causes the murine type of disease *Rickettsia mooseri*

TYPHUS

There are two epidemiologic types of typhus which are determined by the identity of the arthropod vector murine typhus transmitted by fleas from rodent hosts to man and epidemic typhus transmitted from man to man by lice The two types of typhus are similar clinically but epidemiologically they are dissimilar In man the clinical symptoms are similar the epidemic or louse borne form being more severe

CHAPTER XXV

TYPHUS FEVER*

RICKETTSIA DISEASES

Typhus belongs to the group of diseases attributed to Rickettsiae These microorganisms may for the present be classified as falling somewhere between the filtrable viruses on one side and the true bacteria on the other They are minute organisms appearing as coccoid or bacillary forms within the cells of animal tissues They are non motile measure about half a micron in diameter and are readily stained with Giemsa or Castaneda stains appearing as bluish bodies often showing a lavender tinge with Giemsa

Rickettsiae have never successfully been cultivated in media free from living cells but grow readily in tissue cultures In addition to the above characteristics it is important to note that the pathogenic rickettsiae may all be transmitted by arthropods from animal to animal The so called rickettsial diseases are usually regarded as being animal diseases which are transmitted from animal to animal including man by various arthropods As a matter of fact the evidence is equally as good that Rickettsiae are arthropod parasites and that animals are only incidentally infected while acting as a source of food for infected arthropods Whatever may be the original host of the parasite it is known that in some of these diseases the infections are present in certain animals in nature and that species of at least four genera of arthropods may be infected by feeding upon such infected animals In others the evidence indicates that infected animals exist in nature Three of the identified rickettsial diseases which occur in man—typhus Rocky Mountain spotted fever and tsutsugamushi—have been shown to be separate entities although closely related The known arthropod vectors for these

* Prepared by R E. Dyer M D Director National Institute of Health Bethesda Maryland

ters of the disease in the past century In Ireland it was particularly associated with the failure of the potato crops More recently typhus became epidemic in Serbia during World War I when it caused over one hundred thousand deaths in six months It took an estimated toll of upwards of 3 000 000 lives in Russia in the years following the revolution During World War II typhus fever caused epidemics in North Africa and Naples Data on the prevalence in Central Europe during hostilities are not yet available but many cases were found in and around prison camps in Germany in the spring of 1945

In civil populations typhus in its epidemic form occurs most often in the poorer sections of cities where cold and poverty result in a crowded and dirty population Under such conditions lice abound and readily move from one person to another With the introduction of typhus into such a population the disease spreads readily from person to person frequently attacking those in attendance on the sick The morbidity and mortality rates among doctors and nurses is very high

The peak of prevalence of epidemic typhus is in the winter and spring This form of the disease is very severe the case fatality rates varying from 25 to 60 per cent of those attacked

Epidemic typhus has been introduced into America from time to time in the past four centuries in connection with immigration It was present in Mexico shortly after the Spanish conquest probably being introduced with the Spanish troops In North America outbreaks occurred at practically all of the northern Atlantic ports during the 19th century All of these outbreaks were more or less self limited the disease never gaining a permanent lodging in North America as an epidemic disease A form of typhus has been present in New York and Boston for many years under the name of Brill s disease By some this type of typhus is considered to be a recurrence of typhus in immigrants who had their first attacks years before Others are of the opinion that Brill s disease of New York and Boston fits into the picture of the murine form of the disease found particularly in the South Atlantic and Gulf States

THE VECTOR OF EPIDEMIC TYPHUS

For many years it was suspected that the body louse was the transmitting agent of epidemic typhus but it remained a suspicion until 1909 when Nicolle (1) succeeded in transmitting the infection

EPIDEMIC TYPHUS—HISTORY AND EPIDEMIOLOGY

It is possible that typhus may have occurred in human beings in the early civilizations but it is not until the middle ages that a written description of a pestilence is definite enough to warrant the assumption that typhus was present In 1083 an epidemic occurred in Italy which probably was typhus A few years later in 1106 another epidemic apparently of the same disease occurred in Bohemia In both of these epidemics the outbreak followed famine

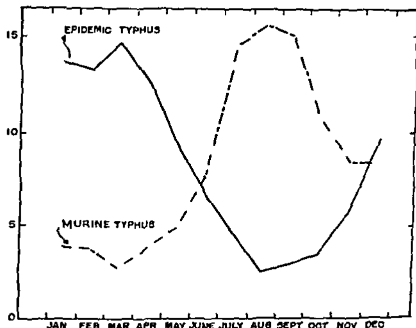


FIG 60—Seasonal distribution of 5331 cases of murine typhus in the United States 1932 1935 compared with 180 000 cases of epidemic typhus in Europe 1930 1935

This tendency for epidemics of typhus to accompany human misery as during war civil revolution and times of famine has been the chief epidemiologic characteristic of this form of the disease The popular names that have been given the disease attest this fact—gaol fever famine fever ship fever In many military campaigns typhus has killed more soldiers than has the enemy—the siege of Granada the Thirty Years War and the Napoleonic campaigns especially the Russian expedition for example In civilian populations Ireland Southeastern Europe and Russia were chief endemic cen

In 1898 Brill first described cases of mild typhus like infection occurring in New York City (3) This infection was later shown to be identical immunologically with louse borne typhus fever but differed from that disease in its epidemiologic characteristics particularly by its lack of communicability failure to be associated with poverty and dirt and the difference in seasonal prevalence As noted above these cases may represent recurrences of previous infections but in any event their description by Brill is the starting point of investigations of mild typhus After the description of mild typhus by Brill cases were described in several of the southern cities from time to time until 1923 when Maxcy undertook a study of this disease in the Southeastern States (4) He found that the infection was fairly common in those States particularly the ports and towns bordering the coast from Baltimore south along the Atlantic and Gulf Coasts and in the Rio Grande Valley In his study he noted an absence of lice a lack of communicability from person to person and no tendency to attack the poorer sections of cities In addition he pointed out that the disease was more prevalent in the late summer and fall and was more apt to occur among those who were engaged in the handling of food stuffs—grocery men warehouse men and the like This latter observation was extended and confirmed by Rumreich who found that a high percentage of the cases investigated by him occurred in men who had lived or worked in rat infested quarters (5)

In recent years there has been an apparent spread of the disease to many of the towns and cities of the interior of the South Atlantic and Gulf States and an extension into certain rural sections of the same States The accompanying map (figure 62) will give an idea of the present distribution of the disease in this country as recognized at present Following the investigations in this country and in Mexico the disease has been described at various places throughout the world—Greece Syria Malaya North Africa South Africa Manchuria and the Hawaiian Islands It is probably more widespread than the above list indicates

RESERVOIR IN NATURE

Many animals chiefly rodents have been found susceptible to typhus and the infection has been recovered from two species trapped in nature—common rats (6) and one species of field mice (7) Since many rodent species are susceptible to the disease it is

to monkeys by means of body lice Head lice have also been shown *capable of transmitting the infection experimentally (2)* but the epidemiologic evidence indicates that the body louse is the principal vector in nature Human body lice feed only upon man and under conditions that bring about the crowding of human beings in close quarters as cold and poverty lice multiply rapidly and pass readily from person to person

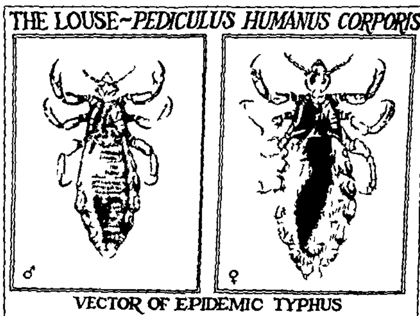


Fig 61

The virus multiplies in the body of the louse in the cells lining the intestine *becoming infectious in four or five days The infection in* the louse reaches its height in about ten days finally killing its host The virus is present in the feces of infected lice and may be transmitted through this medium It has not been definitely shown that the infection can be transmitted by the bite alone The virus is not transmitted through the egg to succeeding generations of lice

HISTORY AND EPIDEMIOLOGY OF MURINE TYPHUS

Just as the epidemiology of epidemic typhus is bound up with the life cycle and feeding habits of human lice so is the epidemiology of murine typhus determined by the life cycle and feeding habits of the rat flea

In 1898 Brill first described cases of mild typhus like infection occurring in New York City (3) This infection was later shown to be identical immunologically with louse borne typhus fever but differed from that disease in its epidemiologic characteristics particularly by its lack of communicability failure to be associated with poverty and dirt and the difference in seasonal prevalence As noted above these cases may represent recurrences of previous infections but in any event their description by Brill is the starting point of investigations of mild typhus After the description of mild typhus by Brill cases were described in several of the southern cities from time to time until 1923 when Maxcy undertook a study of this disease in the Southeastern States (4) He found that the infection was fairly common in those States particularly the ports and towns bordering the coast from Baltimore south along the Atlantic and Gulf Coasts and in the Rio Grande Valley In his study he noted an absence of lice a lack of communicability from person to person and no tendency to attack the poorer sections of cities In addition he pointed out that the disease was more prevalent in the late summer and fall and was more apt to occur among those who were engaged in the handling of food stuffs—grocery men warehouse men and the like This latter observation was extended and confirmed by Rumreich who found that a high percentage of the cases investigated by him occurred in men who had lived or worked in rat infested quarters (5)

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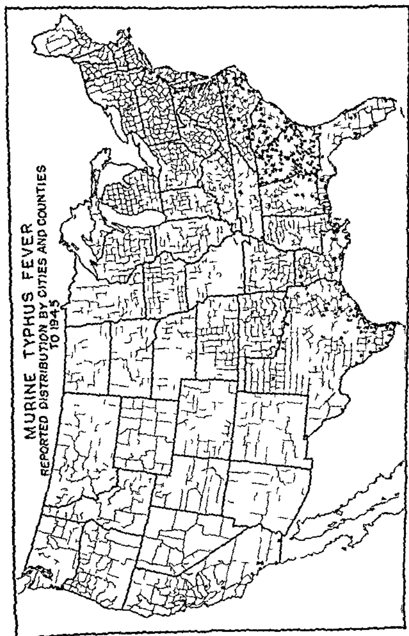

MURINE TYPHUS FEVER
REPORTED DISTRIBUTION BY CITIES AND COUNTIES
TO 1945

Fig 82

probable that the disease may be present in nature in several of them or may extend to other species in the future The animals susceptible to typhus fever are shown in table 47

Table 47—ANIMALS SUSCEPTIBLE TO TYPHUS FEVER

Animals
Laboratory and domestic animals
Cat dog guinea pig rabbit (laboratory) white rat
Animals not native in the United States
Chimpanzee
Monkey—two species (*Macacus sinicus Macacus rhesus*)
Hedgehog gerbil garden mouse wood mouse
Spermophile (*Citellus citellus*)
Squirrel (*Xerus-atlantoxerus-getulus*)
Dwarf mouse (*Mus minutus*)
Meadow mouse (*Microtus terrestris*)
Animals introduced into the United States
Grey rat house mouse
Animals native in the United States
Flying squirrel (*Glaucomys volans saturatus*)
Opossum (*Didelphis virginiana*)
Woodchuck (*Marmota monax monax*)
Cotton rat (*Sigmodon hispidus hispidus*)
Rice rat (*Orzyomys palustris palustris*)
Wood rat (*Neotoma floridana rubra*)
Cotton mouse (*Peromyscus gossypinus gossypinus*)
Golden mouse (*Peromyscus nuttalli aureolus*)
Meadow mouse (*Microtus pennsylvanicus pennsylvanicus*)
Old field mouse (*Peromyscus polionotus polionotus*)
White-footed mouse (*Peromyscus leucopus noveboracensis*)

Subspecies not identified

THE VECTOR OF MURINE TYPHUS

Experimentally it has been shown possible to infect the human louse the rat louse and several species of fleas with murine typhus The evidence at present indicates that the rat flea and the rat louse are the vectors from rodent to rodent and that the rat flea transmits the infection to man Of the species of rat fleas experimentally capable of transmitting the infection the species *Xenopsylla cheopis* is probably the most common vector to man since this species readily bites man when hungry and since the curve of prevalence of this flea fits closely the curve of incidence of the disease in man

The virus has been recovered repeatedly from rat fleas found at or near locations where typhus has occurred in man

Dyer has shown that the rat flea may be infected by allowing it to feed on an infected animal The infection multiplies in the flea reaching its height in two or three weeks The feces of infected fleas are infectious and the infection may gain entrance through flea bites or through abrasions caused by scratching It is possible that the infection may be transmitted by the inhalation of dried flea feces

or by contamination of mucous membranes by such infected material All attempts to transmit the infection by the bite alone have been negative Unlike the louse the flea does not succumb to the infection The virus is not transmitted through the egg to succeeding generations of fleas (8)

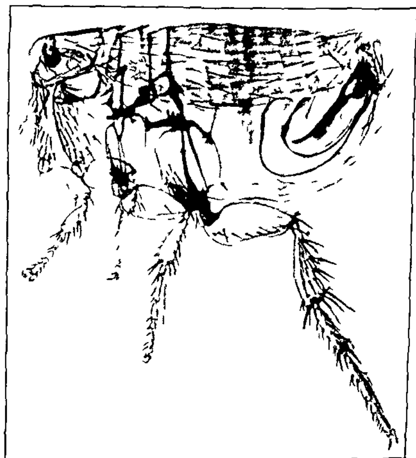


FIG 63—Rat flea *Xenopsylla cheopis* (male)

THE DISEASE IN LABORATORY ANIMALS

Of the animals known to be susceptible to typhus fever the guinea pig is the most satisfactory for experimental use Although excepting the severity of the response there are no recognizable differences in the clinical reaction of man to murine typhus or epidemic typhus there are certain differences in the reaction of guinea pigs to these two types In the murine type a fever develops a few

days after intraperitoneal inoculation of infectious material The duration of this incubation period from the time of inoculation to onset of fever varies somewhat with the material used for inoculation If infectious guinea pig blood is used the incubation period is usually 5 to 9 days in duration occasionally longer The fever is apt to be irregular in type seldom going higher than 40 C to 40 2 C

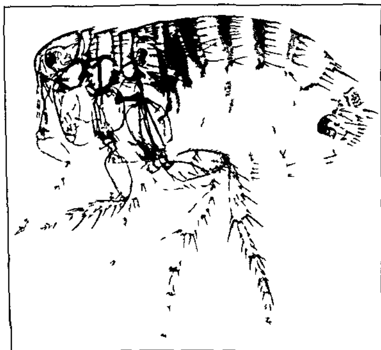


Fig 64 —Rat flea *Xenopsylla cheopis* (female)

and commonly lasts from one to five days Occasionally guinea pigs show fever a few days longer without other evidence of the presence of secondary infections Uncomplicated typhus does not kill the guinea pig Following intraperitoneal inoculation of murine typhus virus into the male guinea pig and usually coincident with the fever there is a swelling of the genitalia and a reddening of the scrotum From oedema of the underlying tissues the *scrotum is* tightly stretched and the testicles can not be pushed through the rings into the abdominal cavity a reduction readily accomplished in the normal animal This involvement of the genitalia usually disappears with the fever Autopsy of animals at the height of the in

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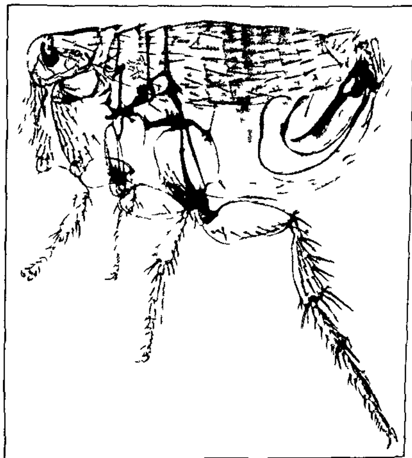


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DIAGNOSTIC AIDS

The Weil Felix reaction is constantly positive in both forms of typhus in man This reaction is the agglutination of certain *B proteus* X strains by the serum of the infected individual The strain of this organism commonly used is known X_{19} and is not concerned with the etiology of the disease The agglutinins appear in the second week and reach their height about the time of defervescence often reaching a titre of 1 1280 or more Titres of 1 320 or less should not be regarded as diagnostic unless the clinical picture is compatible with typhus and other diseases can be excluded Unfortunately for the diagnosis of typhus this reaction is also present in other of the rickettsial diseases In the section of the United States where Rocky Mountain spotted fever and typhus both exist the Weil Felix consequently gives no aid in the differential diagnosis

The complement fixation test using Rickettsiae grown in the yolk sac of the developing chick embryo is proving of greater value in the diagnosis of rickettsial infections and in addition differentiates between spotted fever and typhus

PREVENTION

The prevention of epidemic typhus is based on vaccination and the eradication of the body louse by personal cleanliness—bathing and change of clothing In a measure this makes the prevention of typhus in civil populations a social problem—education and the alleviation of squalor In the control of epidemics of typhus the patients should be freed of all vermin and segregated in surroundings where they may be kept free from vermin Contacts should be deloused and segregated for at least fourteen days Rooms from which typhus patients have been removed should be disinfected to insure the destruction of all lice

The use of the new chemical DDT has proved to be the method of choice for delousing This compound is prepared in a dusting powder which by use of hand or power duster can be thoroughly disseminated in the clothing without disrobing

In the prevention of murine typhus the same measures should be applied which have been found of value in the control of bubonic plague—the destruction of rats and rat harbors The rat flea *Xenopsylla cheopis* when hungry feeds readily upon man These fleas

fection will show a congestion of the blood vessels of both layers of the tunica covering the testicles often with hemorrhages and a filmy exudate on the surface Rickettsiae are readily demonstrable in the cells of this exudate

In guinea pigs infected with epidemic typhus the incubation period is about the same as that noted for the murine type The fever is steadier in that days on which the animal shows no fever are not common The fever usually lasts from 5 to 9 days As in murine typhus the animals do not appear sick and do not die unless other infections are also present Transient reddening and swelling of the scrotum occasionally is seen in guinea pigs infected with epidemic virus but usually this reaction is lacking

Rabbits and monkeys when infected with typhus virus of either form (epidemic or murine) develop the Weil Felix reaction usually with a titre of 1 40 to 1 320 Guinea pigs do not show this reaction

White rats develop a fever following inoculation with the murine virus but fail to do so in response to epidemic virus Rats occasionally develop the Weil Felix reaction in low titres

In white mice the virus of the murine disease can be passed from mouse to mouse indefinitely but the epidemic virus dies out after a few passages in the same species

Complete cross immunity exists between the two types of typhus in laboratory animals

THE DISEASE IN MAN

In man typhus fever runs a febrile course of about fourteen days The most definite diagnostic sign is the rash which appears about the fifth day The rash consists of rose red macules about 2 to 3 mm in diameter which become definitely petechial and darker as the disease progresses The rash first appears over the lower chest or upper abdomen spreading from this location to the upper arms shoulders back and thighs In severe cases the forearms lower legs and palms and soles may be involved The rash seldom includes the face

In the murine form of the disease serious complications are rare and the fatality rate is below 5 per cent with most of the deaths occurring in those over 50 years of age Complications particularly pneumonia are more common in the epidemic disease and the case fatality may reach 60 per cent in severe epidemics

There is no specific treatment of proved value for typhus fever

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spend part of their time away from their normal hosts along rat runs and in the rat nests from which locations they attack man when occasion offers Studies are now under way to determine the value of DDT in the destruction of fleas in murine typhus foci

Vaccines have been prepared against typhus, both in Europe and this country The vaccine with which the American armed forces were inoculated during World War II is prepared from rickettsiae grown in the yolk sac of the developing chick embryo This vaccine has been used on a large scale and the evidence so far accumulated shows that it will definitely modify the severity of a subsequent attack of typhus and as far as is known at present no death from typhus has occurred in a previously vaccinated individual The reactions following the use of this vaccine are usually mild Persons known to be allergic to chicken or to eggs should be skin tested before vaccination to determine sensitivity

ITEMS OF NOTE

1 Typhus fever is one of the Rickettsia diseases
2 There are two epidemiologic types of typhus epidemic or louse borne and murine or flea borne
3 The epidemiologic features of epidemic typhus are
   a greater prevalence in winter and spring
   b communicability from man to man
   c tendency to attack distressed populations
   d association with lice
4 The epidemiologic features of endemic typhus are
   a greater prevalence in late summer and fall
   b lack of communicability from man to man
   c association with rats and rat harbors
5 A known reservoir of murine typhus exists in two species of rodents
6 The rash begins on the body and spreads to the extremities avoiding the face
7 The Weil Felix reaction is present in practically all cases
8 The complement fixation reaction develops uniformly and is a definite aid in diagnosis
9 Prevention and control of epidemic typhus are based on vaccination and delousing
10 Prevention and control of murine typhus are based on the elimination of rat harbors and the destruction of rats and fleas

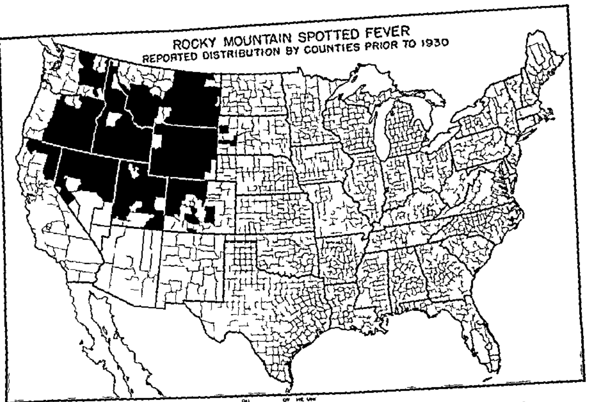


Fig 65 —Distribution of Rocky Mountain spotted fever in the United States prior to 1930

CHAPTER XXVI

ROCKY MOUNTAIN SPOTTED FEVER*

ROCKY MOUNTAIN spotted fever is one of the two rickettsial diseases endemic in the United States (See Typhus Fever Chapter XXV) The rickettsiae described in connection with this disease have been named *Rickettsia rickettsi* or *Dermacentroxenus rickettsi* The disease is transmitted to man by ticks of two or more species

HISTORY

Rocky Mountain spotted fever is known to have been present in certain sections of the northern Rocky Mountain regions at the time that country was first settled by white men It is probable that the disease occurred among the Indians prior to white settlement but no accurate data of that earlier period are available The disease was well recognized among the settlers in the eighties and nineties of the last century but was first noted in the medical literature by Maxey (1) in 1899

Until 1930 spotted fever was thought to be limited to the northwestern states as with the exception of a single case which occurred in Indiana in 1925 (2) no cases had been recognized east of a north and south line drawn through the center of the Dakotas In 1930 the disease was recognized by Rumreich (3) and clinically and epidemiologically differentiated from murine typhus in Maryland and Virginia At the same time Badger (4) by laboratory studies definitely established the identity of the eastern cases with the northwestern cases of spotted fever Later study of the records of earlier cases in the eastern states has led to the conclusion that spotted fever existed in the east for at least fifteen years before recognition More recently a disease described in São Paulo Brazil under the name exanthematic typhus of São Paulo has been found

* Prepared by R F Dyer M D Director National Institute of Health Bethesda Maryland

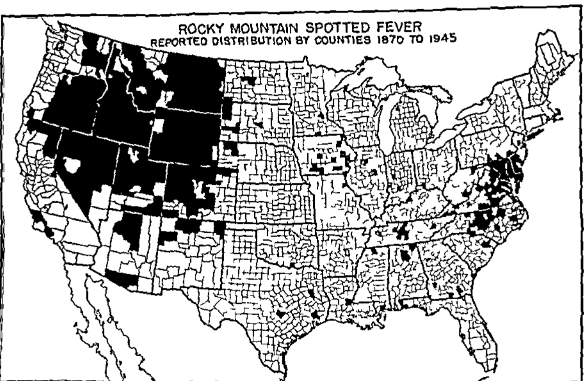


Fig 66 —Distribution of Rocky Mountain spotted fever in the United States to 1945

indistinguishable from Rocky Mountain spotted fever by cross immunity and protection tests (5 6) The disease has also been identified in Colombia and Mexico Other closely related diseases are Boutonneuse fever of the Mediterranean basin Kenya typhus of East Africa and possibly certain of the South African tick fevers

Following the establishment of the fact that spotted fever was not limited to the northwestern states there has been a widespread recognition of cases fairly well over the entire country Including the year 1945 all but a few states had reported the recognition of one or more cases within their borders In addition cases have been recognized in two of the provinces of Western Canada—British Columbia and Alberta

The number of cases recognized annually in the United States is about 1 000 with the greater number occurring in the northwestern states

As in other rickettsia diseases the epidemiology of Rocky Mountain spotted fever in man is dependent upon the life history and feeding habits of the vector in this instance a tick The disease occurs most frequently among those whose occupations expose them to the bites of ticks such as sheepherders agricultural workers surveyors foresters and the like A number of cases occur each year among campers vacationists picnickers and others whose occupations or pleasures take them into the rural areas Occasional cases occur in urban dwellers from contact with ticks in vacant lots or with ticks brought home by pets In several instances persons have acquired the infection by crushing ticks with their fingers while removing them from dogs The great majority of cases of spotted fever occur in the late spring and early summer with an occasional case developing in the late summer and fall There is some variation in this seasonal prevalence in the different sections of the country In the northwest the disease is practically limited to the months March to July inclusive with April May and June the months of greatest incidence In the states along the Atlantic seaboard cases occur during the same months noted for the northwest with an extension to include the first part of August The season of greater incidence in the east falls a little later than in the west the months of May June and July being the height of the spotted fever season

Age and sex have no influence on susceptibility to the disease There is a greater incidence among males than females and among children of both sexes than among adult females a fact which is

ting the infection to their tick parasites The list of animals found susceptible embraces several species of rodents squirrels rats mice rabbits and woodchucks and of the larger animals the dog and the sheep It should be noted that the dog is possibly the chief reservoir of boutonneuse fever which is closely related to spotted fever

THE VECTOR

The role of ticks in the transmission of Rocky Mountain spotted fever was largely worked out by Ricketts (8) in 1906 prior evidence being supplied by the work of McCalla (9) Wilson and Chowning (7) and supplemental data added by the work of Fricks (10) Spencer and Parker (11) and others King (12) experimentally transmitted the disease by ticks about the same time that Ricketts successfully carried out the same experiments Ticks of several species have been found capable of being infected and of transmitting the infection experimentally while infected ticks of three species have been found in nature

Tick species found infected in nature are

- Western Wood Tick (*Dermacentor andersoni*)
- Eastern Dog Tick (*Dermacentor variabilis*)
- Rabbit Tick (*Haemaphysalis leporis palustris*)

In addition to the three species listed above the following species have been shown to be capable of transmitting the infection experimentally

- Pacific Coast Tick (*Dermacentor occidentalis*)
- Brown Dog Tick (*Rhipicephalus sanguineus*)
- Lone star Tick (*Amblyomma americanum*)
- Cayenne Tick (*Amblyomma cajennense*)
- Rabbit Dermacentor (*Dermacentor parumapertus*)

Of the above ticks *D andersoni* and *D variabilis* are of the greatest importance in transmitting the disease to man in this country while the others with the exception of the two rabbit ticks are potentially important though not definitely convicted of causing human infections Accumulated evidence indicates that the rabbit tick *Haemaphysalis leporis palustris* although not feeding on man plays possibly a greater part than any other tick in the dissemination of this disease in nature being the only tick which occurs in all parts of this continent where spotted fever has been recognized in man

In each of the species listed above the experimental data show

explained by the greater risk of exposure to ticks by reason of the occupations of adult males and the more frequent excursion of children into tick infested areas in the course of their play

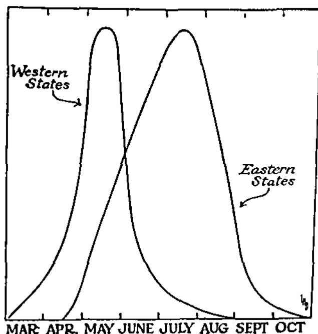


FIG 67—Seasonal distribution of Rocky Mountain spotted fever in the United States

In general it may be stated that all cases occur following conditions under which exposure to ticks was probable and that definite history of tick contact (bites or crushing of ticks) precedes the onset of the disease in man in the great majority of cases

SUSCEPTIBLE ANIMALS

Studies made by Wilson and Chowning (7) in 1902 led to the conclusion that a reservoir of Rocky Mountain spotted fever existed in nature in rodents and despite the fact that the virus of the disease has never been recovered from a wild animal it is undoubtedly true that infected animals do exist in nature and play an important part in the perpetuation of the disease since protective antibodies have been demonstrated in the blood of certain wild rodents (11) Laboratory studies have shown that many species of animals are susceptible to the virus and while infected are capable of transmit

to engorgement taking seven to ten days The female increases enormously in size during feeding and after becoming detached she drops to the ground lays her eggs two to six thousand in number and dies without feeding again From the eggs hatch six legged larvae These larvae find a host presumably in most instances a small rodent and feed to engorgement during a period of four to six days The larvae then detach drop to the ground and after a short period of sluggish activity become quiescent and moult to eight legged nymphs These nymphs in their turn find a host and feed to engorgement taking six to eight days in the process They then moult to the eight legged adult male and female

In nature these ticks pass the winter in one of the flat or unfed stages and probably consume two years in completing the cycle from adult to adult Unfed adult ticks are said to be able to survive up to four years

The percentage of infected ticks found in nature varies from year to year in known infected localities In certain small sections of the northwest the percentage of ticks examined and found infected has reached two per cent in certain years while no infected ticks have been found in the same areas in other years Out of about one thousand ticks taken from small areas in the east where spotted fever was occurring in human beings the virus has been recovered surely only once

THE DISEASE IN LABORATORY ANIMALS

Rhesus monkeys rabbits white rats and guinea pigs are susceptible to Rocky Mountain spotted fever and of these the guinea pig is the most satisfactory for experimental or diagnostic investigations

To establish the infection in guinea pigs from a human case 2 to 4 c c of blood taken from the patient at the height of the disease should be injected intraperitoneally In examining ticks for the presence of the infection they may be ground up in a mortar suspended in a little saline and this suspension injected into the guinea pigs intraperitoneally Experience has shown that attempts to disinfect the outside of the ticks prior to grinding them up are unnecessary as secondary infections of the animals seldom follow the injecting of ticks without preliminary disinfection

The incubation period in guinea pigs following intraperitoneal injection of blood varies somewhat with the virulence of the virus strain The highly virulent strains present in certain sections of the

that stage to stage transmission of spotted fever virus takes place In other words the infection may be acquired by the tick in one stage of its life cycle and retained through subsequent moults to succeeding stages and from infected adult females through the egg to the larvae

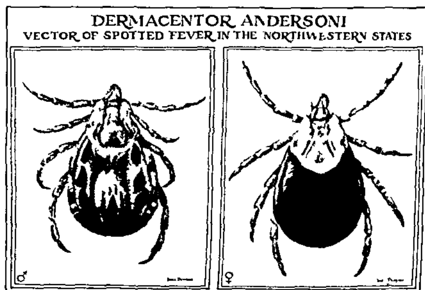


Fig 68

The two ticks held accountable for most of the human cases of spotted fever in this country *D andersoni* and *D variabilis* are three host ticks spending the periods between feedings away from the hosts The larval or nymphal stages are found on the smaller animals especially rodents while the adults are found more frequently on the larger animals wild and domestic The adult tick conveys the infection to man since the two immature stages are seldom found on man

The known distribution of *D andersoni* includes the states of Washington Oregon Idaho Montana Wyoming Nevada Utah Colorado northern sections of California New Mexico and Arizona and the extreme western part of South Dakota while *D variabilis* has been reported from the remaining states of the Union California Colorado Oregon South Dakota and Montana have reported both species

The life cycle and feeding habits of the two Dermacentors are as follows The adult tick normally attaches to one animal and feeds

to engorgement taking seven to ten days The female increases enormously in size during feeding and after becoming detached she drops to the ground lays her eggs two to six thousand in number and dies without feeding again From the eggs hatch six legged larvae These larvae find a host presumably in most instances a small rodent and feed to engorgement during a period of four to six days The larvae then detach drop to the ground and after a short period of sluggish activity become quiescent and moult to eight legged nymphs These nymphs in their turn find a host and feed to engorgement taking six to eight days in the process They then moult to the eight legged adult male and female

In nature these ticks pass the winter in one of the flat or unfed stages and probably consume two years in completing the cycle from adult to adult Unfed adult ticks are said to be able to survive up to four years

The percentage of infected ticks found in nature varies from year to year in known infected localities In certain small sections of the northwest the percentage of ticks examined and found infected has reached two per cent in certain years while no infected ticks have been found in the same areas in other years Out of about one thousand ticks taken from small areas in the east where spotted fever was occurring in human beings the virus has been recovered surely only once

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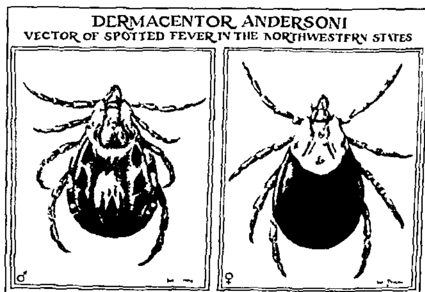


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tite listlessness and headache The onset is usually sudden with a chill or chilly sensations and rapidly rising fever Prostration is usually marked In the more severe cases nosebleed may occur early Soreness of the muscles and joints is commonly present The temperature rises rapidly and reaches its highest point usually in the second week The termination is by rapid lysis after a febrile period of about three weeks

The most distinguishing characteristic of the disease is the rash This appears between the second and fifth days usually on the third or fourth The eruption is macular rose red in colour at first and becomes fainter almost disappearing during the morning remission of fever early in the disease The macules become more distinct each day becoming definitely petechial early in the second week in all but the mildest cases In the severe cases the spots become deep red or purplish and confluent Necroses may develop The rash usually persists throughout the febrile period and into convalescence becoming brownish in colour A branny desquamation often occurs over the areas where the rash was thickest The site of the first location of the rash and its spread and final distribution are important in the diagnosis of the disease The rash first appears usually on the wrists and ankles It spreads rapidly in the first twenty four to forty eight hours to the back then arms legs chest and last to the abdomen where it is least marked The palms and soles are frequently involved and occasionally the face and the scalp are included

PREVENTION

Methods for prevention of spotted fever have been directed at the eradication of ticks To date these attempts have not been very successful The difficulty of the problem may be recognized when the variety of hosts on which this parasite may feed is considered In Montana the poisoning of rodents has been tried in the hope of limiting the food supply available for the immature stages of the ticks The adult ticks have been attacked by the dipping of domestic stock The clearing away of brush and the burning over of tick infested areas are doubtless of assistance in reducing the number of ticks both by removing common sources of food for the ticks and by actual destruction of the ticks themselves A tick parasite was introduced into Montana some eight or nine years ago but a longer period of time must elapse before a decision as to the value of this measure can be reached

northwest produce the disease in guinea pigs two to three days after inoculation These animals show listlessness, progressive loss of weight and high fever usually 105°F or a little above About 90 per cent of the animals die around the end of the first week If the animal survives defervescence occurs after a variable period of five to fifteen days In a majority of male guinea pigs infected with the virulent strain a scrotal reaction develops about the third day of fever This reaction begins as a macular rash on the skin of the scrotum Oedema of the underlying tissues and swelling of the testicles are absent on gross inspection the reaction being largely confined to the skin The rash becomes petechial and coalescence of the spots occurs As the reaction progresses necrosis of the affected skin areas follows which is in turn followed by sloughing As the guinea pig recovers healing takes place by scar formation Necrosis of the tips of the ears frequently occurs At autopsy of guinea pigs at the height of the infection the most noticeable finding is an enlarged and darkened spleen This organ is enlarged in all diameters and may be from two to five times its normal size

In less virulent strains in guinea pigs the percentage of deaths may fall as low as 5 per cent and the scrotal reaction be absent Of the strains isolated in guinea pigs from human cases and from ticks east of the Mississippi River none has shown the scrotal reaction seen in certain virulent western strains The strains from São Paulo Brazil have shown scrotal reactions identical with those caused by virulent western strains of the United States

Monkeys and rabbits develop the Weil Felix reactions when infected with spotted fever Monkeys often develop a rash similar in character to the rash seen in human cases The rash in monkeys is found on the face over the lower back and the outside of the thighs Necrosis of the ears sometimes occurs in monkeys Virulent spotted fever is highly fatal in monkeys

Rabbits develop a fever and quite frequently show a scrotal reaction similar to that seen in guinea pigs

THE DISEASE IN MAN

The diagnosis of spotted fever in the human being is usually made on clinical grounds and the complement fixation test

In man the disease has an incubation period of two to twelve days most often being a week or a little less The actual onset may be preceded by a few days of ill defined prodromata—loss of appe

spring and early summer although out of season cases do occur

8 Ticks once infected remain so for life and pass the virus to succeeding generations

9 The prevention of the disease is largely one of personal care in avoiding ticks plus the use of vaccine in known infected areas where it is not feasible to avoid ticks

10 A serum has been developed which is of value in treatment

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Two types of vaccines have been prepared for spotted fever One method utilizes rickettsiae harvested from infected ticks More recently a vaccine similar to the typhus yolk sac vaccine has been developed In the production of immunity there is no choice between the two vaccines The yolk sac vaccine should be avoided if sensitization to chicken or egg is present in the individual to be vaccinated Sensitization to ticks occurs but is relatively uncommon

Vaccine may be administered to those whose occupations expose them particularly to tick bites in known infected areas Two or three inoculations of the vaccine give a degree of protection usually sufficient to last through one tick season but the immunity apparently is not permanent Occasional cases of spotted fever have developed in vaccinated persons but the vaccine apparently lessens the severity of the disease and seems to insure recovery For its full protective value the vaccine should be taken at least ten days before exposure to tick bite The vaccine is of no value in the treatment of the disease

Probably the most effective method of prevention is the exercise of personal care Known infected areas should be avoided insofar as possible during the tick season Those who must visit such areas should frequently examine their clothing and body for ticks The tick usually does not become attached to its host at once but often times crawls around for several hours It has been shown also that the chance of receiving infection from the bite of an infected tick is directly proportional to the length of time the tick has fed on the exposed individual

ITEMS OF NOTE

1 Rocky Mountain spotted fever is one of the Rickettsial diseases
2 It has been recognized in most states of the United States and in Brazil Colombia Mexico and Canada
3 The disease is transmitted to man by ticks
4 Several species of ticks are capable of transmitting the infection The two most important species in the United States are *D andersoni* in the northwest and *D variabilis* in the east
5 Animals furnish food supply for ticks and infected animals probably exist in nature
6 The disease is not transmitted from person to person
7 The disease is rural in nature and is practically limited to the

GEOGRAPHIC DISTRIBUTION

Tsutsugamushi disease has been found over a wide spread area in the Asiatic Pacific region Originally it was thought to be confined to Japan but later experience showed that it existed also in China Korea Nansei Islands Formosa Pescadores Islands Philippine Islands Indo China Cambodia Malay Peninsula Ceylon Maldive Islands Sumatra Java Borneo New Guinea North Queensland (Australia) Bako Islands Burma and India

There are probably other areas also where the disease exists There is also the possibility, because the vector is a mite that areas now known to be free of the disease will later become infected The disease is tropical in nature however and according to Cook (7) does not occur at temperatures less than 65 F

SEASONAL PREVALENCE

No seasonal variation in the incidence of tsutsugamushi disease occurs in the tropics In cooler climates such as Japan and Formosa a seasonal variation has been noted with cases occurring mostly during the months of July and August

ETIOLOGIC AGENT

The etiologic agent of tsutsugamushi disease is *Rickettsia orientalis* (*R nipponica R tsutsugamushi R akamushi*) Black and his coworkers (1) confirmed the rickettsial nature of the organism in New Guinea Early in the course of the illness it can be recovered from the patient s blood stream Injection of white mice produces a fatal infection and intra and extra cellular bodies frequently occurring in pairs may be demonstrated in Giemsa stained smears

Cultures in bacteriological media (broth or agar slants) remain sterile but the organism may be grown on yolk sac tissue of fertile hens eggs in a manner similar to the other rickettsia of the typhus group

Strains of *R orientalis* isolated from different geographic areas vary in virulence but are identical in cross immunity tests

MITE VECTORS

Tsutsugamushi disease is transmitted by the bite of the larval form of a mite of the genus *Trombicula* In the development of the mite from the egg to the adult only the larval forms are parasitic on

CHAPTER XXVII

TSUTSUGAMUSHI DISEASE
(Mite Typhus)

Tsutsugamushi disease is an infection of rodents, caused by *Rickettsia orientalis* Man is infected by the bite of the rat mite

HISTORY

Tsutsugamushi disease has been known according to Williams (3) since the sixth century In an extensive review of the literature Blake Maxcy Sadusk Kohls and Bell (1) state that it was encountered by the natives of South China in the 16th century

Hashimoto described the disease in Japan in 1810, calling it tsutsuga Palm in 1878 added further evidence calling it "shima mushi The next year Baelz showed that it was caused by the bite of a mite Clinical and epidemiological evidence was added by Tanaka in 1899 and later by workers of the Kitasato Institute for Infectious Diseases Kitashima and Miyajima in 1918 demonstrated that field mice in Japan were rodent hosts The etiologic agent was suspected by Hayoshi in 1920 and named *Rickettsia tsutsugamushi* Various other workers described the organisms under other names Nagayo and his associates in 1930 identified it under the name of *Rickettsia orientalis*

Little attention was paid to the disease in occidental countries up to the Second World War when American troops invaded the islands of the Southwest Pacific Ocean

Among the various designations by which the disease has been known are tsutsugamushibyo shimamushi Japanese river fever flood fever kedani fever mite fever, scrub typhus (K form) rural typhus tropical typhus pseudo typhus and Mossan fever (3) By priority tsutsugamushi disease is the accepted term By common usage scrub typhus and mite typhus are more popular

Trombicula minor in Australia and New Guinea
Trombicula acuscutellaris in India

Numerous species of mites infest rodents in the Orient and islands of the Southwest Pacific and additional investigation has shown that others than those listed above are capable of transmitting tsutsugamushi disease Some mites are merely nuisances causing a severe dermatitis called scrub itch In North America *Trombicula irritans* causes "harvest itch

Ticks such as the genus *Amblyomma* in Sumatra have been suspected in the transmission of this disease but evidence is lacking

RODENT HOSTS

A variety of rodent hosts of tsutsugamushi disease are found in nature Rickettsial organisms have been found in the following rats (3) –

Melomys littoralis *Rattus assimilis* *Rattus conatus* *Rattus norvegicus* (white strain) *Rattus norvegicus* (black & white strain) *Rattus rattus* *Rattus losea* *Rattus concolar browni* and *Mus rattus rufescens* The vole *Microtus montebelli* and the bandicoot *Isoodon torosus* also carry the organisms Numerous other rodents are infested with mites and experience may show that they are reservoirs of rickettsial infection

The laboratory animals which are subject to infection include white mice white rats guinea pigs and rabbits

Birds have been reported as possible hosts of the disease since they are infested with mites but this has not been confirmed Wild birds are capable however of distributing infected mites over wide areas and to distant countries in migration

Mites feed upon dogs cats wild pigs swamp hens bush fowls parrots buffaloes monkeys lizards and probably many other animals Gunther lists seventeen such hosts Few of them probably compare with rodents as reservoirs of tsutsugamushi disease

THE DISEASE IN MAN

The mites which cause tsutsugamushi disease attack regions about the waistline scrotum groin and armpits where they find the moisture favorable The most common site of the primary lesion according to Ahlm and Lipshutz (4) is found in the scrotal area though the inguinal and ankle areas are frequently involved Cook

vertebrate hosts The metamorphosis from larva to nymph requires a meal of blood from the host The nymph and adult forms are not parasitic on man or animals but live on the ground feeding on plants The adults lay their eggs on the ground, where the new larvae hatch out

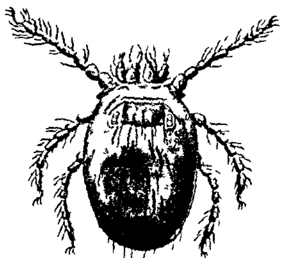


Fig 69 —Kedani mite *Trombicula akamushi* Courtesy Sharp and Dohme

The larval forms which attack man are reddish in color but of almost microscopic size about 0 2 to 0 3 mm in length They are six legged resembling tiny spiders They attach themselves to the skin by means of their hooked mouth parts One meal of blood is all that is necessary for the metamorphosis from larva to nymph and apparently the larva does not feed a second time If the larva of a previous generation however has fed upon an infected rodent the new larva will probably be capable of causing infection in the new host for the rickettsiae are transmitted through the egg from generation to generation

Williams (3) lists the following mites responsible for the transmission of tsutsugamushi disease

Trombicula akamushi in Japan China Formosa Malaya Pescadores Islands and Sumatra

Trombicula deliensis in Australia India Malava New Guinea and Sumatra

At the earliest time possible after exposure a bath should be taken with thorough soaping and scrubbing of the skin

D D T is not effective against mites

ITEMS OF NOTE

1 Tsutsugamushi disease is one of the Rickettsia group of diseases caused by *Rickettsia orientalis*
2 The disease exists over a large area of Southeast Asia from Korea to India and in the islands of the Southwest Pacific from Japan to northern Australia
3 The vector is the rat mite *Trombicula akamushi* or related species
4 Only the larval forms of the mite are parasitic and transmit the disease
5 Mites once infected pass the rickettsia on to the next generation through the egg
6 The reservoir of infection is found in wild rats and mice
7 Mortality in persons suffering from the disease varies from two to ten per cent depending on such factors as age condition of the patient etc
8 Prevention consists in protection against mite bites There is no protective vaccine

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(7) found 92 per cent on the trunk arm or thigh The bite is pain less and usually overlooked

The primary lesion or eschar, where the mite causes the infec tion has a pinched out appearance about three to ten mm in diameter covered with a black crust and surrounded by a small erythematous border (5) After an incubation period of seven to fourteen days the patient suffers from headache backache weak ness chilliness fever and insomnia The fever rises to about 104°F or 105°F About the fourth or fifth day after symptoms appear there is a macular or maculopapular rash on the trunk Mild cases begin to improve in twelve to fourteen days Severe cases may develop atypical pneumonia or encephalitis

Diagnosis is confirmed by the appearance of the eschar, when it can be found by the recovery from the blood stream of *R orientalis* during the febrile period and by a positive Weil Felix test with Proteus OXK after the twelfth or fourteenth day of illness A nega tive Weil Felix reaction does not rule out the disease however

Various other diseases occur in regions where tsutsugamushi dis ease is found such as malaria dengue and infectious hepatitis which make a differential diagnosis difficult

The mortality rate varies from two to ten per cent depending on various factors such as age the condition of the patient etc Above the age of forty years the mortality rate is much higher Tsutsu gamushi disease is not transmitted from person to person

PREVENTION

There is no protective vaccine against tsutsugamushi disease Persons going into mite infested areas where the disease exists incur some risk of infection This risk may be minimized by precautions learned by the military forces during World War II

Camp sites should be cleared of grass and debris the ground burned over and then sprayed with oil Cots or hammocks should be used for sleeping purposes rather than the ground Clothes should be sprayed or rubbed with an anti mite fluid such as dimethyl phthalate or dibutyl phthalate McCulloch found that dibutyl phthalate was very efficient At a dosage rate of one fluid ounce per set of clothes it gave protection for 22 days the clothes being *washed 8 times* in cold water during that period (8) The hands should be smeared with an anti mite fluid at frequent intervals when in tick infested areas, and care should be taken to protect the ankles

VECTORS

The tick of chief importance in Australia in the spread of Q fever is *Haemaphysalis humerosa* but there are several other possible vectors (table 48) *H humerosa* probably is an important source

Table 48 —TICKS OF POSSIBLE SIGNIFICANCE IN THE TRANSMISSION OF Q FEVER IN AUSTRALIA (DERRICK 8)

TICK	PRINCIPAL HOST	OTHER REPORTED HOSTS	RELATION TO Q FEVER
Haemaphysalis humerosa	Bandicoot	*Rattus rattus* *Rattus culmorum youngi* opossum cattle horse	Proved vector among bandicoots
Haemaphysalis bispinosa	Cattle	Sheep horse dog man	Potential vector
Boophilus annulatus microplus	Cattle	Sheep	Can be infected
Ixodes holocyclus	Bandicoot	Most bush and domestic animals and man	Probable vector
Rhipicephalus sanguineus	Dog	Sheep cattle horse cat man	Potential vector
Ornithodorus gurneyi	Kangaroo	Man	Can be infected Unlikely vector

of infection among bandicoots but it does not bite man A possible method of human infection is inhalation or wound contamination with the dried feces of the tick The rickettsiae are confined to the lining of the epithelium and the lumen of the gut and the feces are highly infective Hereditary transmission of the rickettsiae has not been demonstrated in *H humerosa*

In the United States the rickettsiae have been found in nature in nymphal and adult forms of the lone star tick *Amblyomma americana* in Texas and the wood tick *Dermacentor andersoni* in Montana and Wyoming Experimental transmission has been accomplished with the argasid ticks *Ornithodoros moubata* and *O hermsi* The former remained infective for 670 days and transmitted the virus through the egg the latter conserved the rickettsiae in the tissues for 979 days but failed to pass the infective agent through the egg in the few experiments tried

ANIMAL RESERVOIRS

The chief reservoir of Q fever in Australia is the bandicoot a small marsupial Agglutination tests showed thirty four per cent were infected in nature (8) Derrick (9) found other bush animals (two marsupials and seven rodents) susceptible to infection how

CHAPTER XXVIII

Q FEVER

Q FEVER is a rickettsial disease in which ticks are involved in the transmission The bandicoot and other animals in Australia are reservoirs of infection In the United States the etiologic agent is identical with that found in Australia

HISTORY

The occurrence of an obscure fever among meat workers and slaughter house employes in Brisbane Australia in 1935 was studied by Burnet and others of the Queensland Department of Health The disease was designated as Q fever (1) and the causative agent was designated as *Rickettsia burneti* (2)

In 1938 Davis and Cox (3) in the United States reported the isolation of ricksettsia organisms from wood ticks collected near Nine Mile Creek Montana and Dyer (4) reported the first case of human infection The disease was designated as American Q fever and the organism as *Rickettsia diaporica* (5)

The organisms encountered in Australia and in the United States were shown to be identical by Dyer (6) and Bengston (7)

GEOGRAPHIC DISTRIBUTION

Q fever has been encountered in Australia almost all the cases being confined to Queensland In the United States cases have been reported in the Pacific Northwest Texas Illinois and in Washington D C where a laboratory outbreak occurred

ETIOLOGIC AGENTS

The cause of Australian Q fever *Rickettsia burneti* and of American Q fever, *R diaporica* are identical by immunologic tests They are similar to other members of the *Rickettsia* group in morphology and staining reactions

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The outbreak among laboratory workers in the United States was probably airborne from infected animals or possibly from dried feces of infected ticks The pneumonia which accompanied the disease in this outbreak would indicate this route of infection

The treatment of Q fever is symptomatic

PREVENTION

The prevention of Q fever is difficult because complete knowledge concerning the epidemiology of the disease is lacking For the present precautions against ticks must be emphasized

ITEMS OF NOTE

1 Q fever is caused by the *Rickettsia burneti* (*R diaporica*)
2 It is transmitted by ticks or through tick feces
3 It has been encountered only in Australia and the United States
4 Bandicoots cattle and rodents are the chief reservoirs of infection in Australia in the United States cattle and sheep have caused the disease
5 Infection through the respiratory route results in an atypical pneumonia infection through the skin is manifested by fever headache and chills lasting one to three weeks
6 The death rate is very low
7 Prevention is difficult due to inadequate knowledge of the epidemiology of the disease

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ever, and he considers them factors in spreading the disease Experimental infection in all of them was mild and often inapparent

Cattle are a common source of human infection in Australia Calves experimentally infected show a brief mild illness Dairy cows tested in an endemic area showed 1 4 per cent positive by agglutination tests Infections were inapparent

In the United States the disease has been traced to cattle and sheep Monkeys rabbits guinea pigs, rats and mice lend themselves to experimental infection

THE DISEASE IN MAN

In Australia there were recognized 176 cases of Q fever between 1935 and 1942 Ages ranged from ten years to sixty four years There was no seasonal incidence The majority of the patients were associated with slaughter houses, but some of them worked on dairy farms or followed other rural pursuits There was no evidence of transmission from person to person Three patients died

The disease manifested itself by an acute onset with chills prostration and fever Headache was pronounced in most cases The fever was continuous lasting from a few days to two or three weeks There was no pulmonary involvement in the Australian cases

In the United States, a few sporadic cases occurred in 1938 in the Pacific Northwest In Washington D C 15 laboratory workers at the National Institute of Health were afflicted in 1940 All showed signs of an atypical or virus pneumonia The disability lasted from 10 to 14 days with no deaths (10)

An outbreak among cattle handlers took place in 1946 in Amarillo Texas with more than 40 cases and 2 deaths (12) In Chicago a few months later there were 9 cases among sheep handlers No deaths occurred

The method of infection in Q fever is not always clear In the Australian cases ticks were without doubt the chief cause of the disease Slaughter house workers might possibly be infected through abrasions from the blood or tissues of the animals they handled but this is a rather unimportant method considering the low infectivity of cattle It is presumed that the ticks found on cattle, especially *Boophilus annulatus microplus* and *Haemaphysalis bispinosa* were the responsible agents Crushed ticks or tick feces are possible sources of infection

The outbreak among laboratory workers in the United States was probably airborne from infected animals or possibly from dried feces of infected ticks The pneumonia which accompanied the disease in this outbreak would indicate this route of infection

The treatment of Q fever is symptomatic

PREVENTION

The prevention of Q fever is difficult because complete knowl edge concerning the epidemiology of the disease is lacking For the present precautions against ticks must be emphasized

ITEMS OF NOTE

1 Q fever is caused by the *Rickettsia burneti* (*R diaporica*)
2 It is transmitted by ticks or through tick feces
3 It has been encountered only in Australia and the United States
4 Bandicoots cattle and rodents are the chief reservoirs of infec tion in Australia in the United States cattle and sheep have caused the disease
5 Infection through the respiratory route results in an atypical pneumonia infection through the skin is manifested by fever headache and chills lasting one to three weeks
6 The death rate is very low
7 Prevention is difficult due to inadequate knowledge of the ep idemiology of the disease

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CHAPTER XXIX

JUNGLE YELLOW FEVER *

YELLOW FEVER is a specific virus infection of vertebrates transmitted by blood sucking invertebrates Long known as a human urban and maritime disease it has within the past 15 years been shown to be basically a disease of forest inhabiting primates with some evidence implicating certain marsupials and rodents as factors in its maintenance Among blood sucking arthropods evidence of ability to transmit the yellow fever virus has been found only in the case of certain mosquitoes Infected mosquitoes carry the infection for life but do not pass it to the next generation The infection in vertebrates is never chronic nor does a carrier state occur The persistence of the virus in a region apparently depends on an unbroken chain of self limited infections in vertebrates infecting successive generations of vectors

Epidemiologically yellow fever may be considered as being

(1) A human disease with transmission occurring in or near the house and with man to man transference responsible for maintaining the virus

(2) A jungle disease with transmission to man occurring in or near the forest and with animal to animal transference responsible for maintaining the infection

Because the *Aedes (Stegomyia) aegypti* mosquito is the traditional vector of urban yellow fever the human disease has in the Americas been called aegypti transmitted yellow fever to distinguish it from jungle yellow fever, a more general term should be used however since in Africa the *Aedes aegypti* mosquito is often present at least in small numbers in areas where the jungle disease exists and important outbreaks of the human disease with transmission from man to man in or near the house may occur in which aegypti is not necessarily the only or even the principal vector

* Prepared by Fred L. Soper M D Dr P H The Rockefeller Foundation

HISTORY

In 1881 Finlay suggested and in 1900 Reed and his co workers proved that the traditional urban and maritime yellow fever is mosquito borne *Aedes (Stegomyia) aegypti* being the vector Antimosquito campaigns in Cuba Brazil Panama Mexico and the United States were followed by the spectacular disappearance of yellow fever not only in the cities worked but also in the smaller communities of the surrounding regions By 1927 yellow fever was apparently limited in the Americas to a small section of north eastern Brazil But the appearance of the disease during the next few years at widely separated points in South America which had no easy means of communication with one another or with the known infected districts of northeastern Brazil showed that there were still unknown elements in its epidemiology

Rio de Janeiro the beautiful capital of Brazil which had been free of yellow fever for 20 years after having paid heavy tribute to the disease from 1850 to 1908 was the first of these points to suffer in 1928 In 1929 yellow fever was confirmed at Socorro Colombia and at Guasapati Venezuela and in 1932 at Santa Cruz de la Sierra Bolivia buried in the center of the continent The traditional vector *Aedes aegypti* was found in all these places and was un doubtedly responsible for the recorded urban outbreaks but the source of the virus which initiated the outbreaks could not be determined

In the meantime yellow fever virus had been established in laboratory animals (*Macacus sinicus* and *Macaca mulatta*) in 1927 and various monkeys and certain mosquitoes of both Africa and South America had functioned in the laboratory as vertebrate and invertebrate elements in the yellow fever infection cycle

In 1932 a rural outbreak of yellow fever occurred in the Vale do Canaan in the State of Espirito Santo Brazil in the absence of *Aedes aegypti* This outbreak has been followed by others in Brazil Colombia Peru Paraguay Bolivia and Venezuela in which aegypti could not be incriminated In 1934 field studies indicated that cases were almost entirely limited to persons having close contact with the forest neutralization tests on wild monkeys showed that the disease was present in the forest In 1935 *Haemagogus capricornii* was incriminated by epidemiological investigations as being a probable mosquito vector Attempts to capture infected mosquitoes

oriented by the occurrence of human cases, were unsuccessful until 1938 when infected *Haemagogus capricornii Aedes (Finlaya) leucocelaenus* and an unidentified sabethine were captured in the forests of the State of Rio de Janeiro Brazil In 1944 virus was isolated from naturally infected marmosets captured at Ilheos, Bahia Brazil

On the other hand continued observation in northeastern Brazil the only area where yellow fever was known to persist in 1927 has failed to implicate vertebrates other than man or any vector other than the aegypti mosquito in the transmission of yellow fever in this region The infection disappeared in 1934 following an intensive rural anti aegypti campaign Yellow fever in the Americas has during the succeeding years been limited to the jungle disease and an occasional small aegypti transmitted outbreak secondary to the jungle infection

In Africa renewed interest stimulated by the findings in South America has resulted in observations indicating that there also yellow fever is basically a disease of the forest although it seems probable that man to man transmission by mosquitoes other than aegypti may be more frequent than in America

GEOGRAPHIC DISTRIBUTION

While at one time or another during the 18th or 19th centuries every country in the Americas suffered inroads of yellow fever no evidence exists of the presence of the disease in North America in the West Indies or in Central America north and west of the Panama Canal since 1925 During the past two decades urban yellow fever has been observed in Brazil Colombia and Venezuela Evidence that jungle yellow fever has been present during the same period in Panama Colombia Venezuela the Guianas Ecuador Peru Bolivia Brazil Paraguay and Argentina has been obtained by neutralization tests or by microscopic examination of liver tissue removed routinely by viscerotomy from the bodies of persons dying after less than 11 days of illness (Fig 70)

In Africa the line has not been so closely drawn between aegypti transmitted and jungle yellow fever Before 1930 yellow fever in Africa was apparently limited to the west coast extending for an unknown distance into the interior Neutralization tests indicate that the disease has existed in recent times in French West Africa

Gambia Sierra Leone Liberia the Gold Coast Nigeria French Equatorial Africa the Belgian Congo Angola Northern Rhodesia

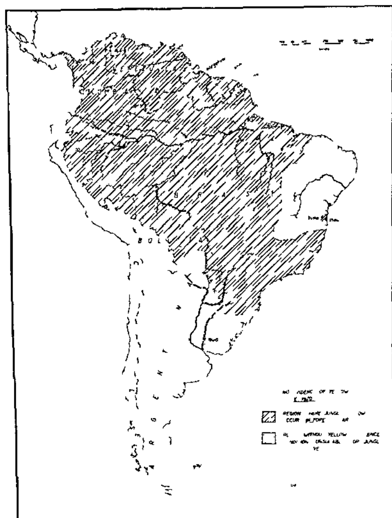


Fig 70—Yellow Fever Areas of South America

Uganda Kenya the Anglo Egyptian Sudan Ethiopia Eritrea and French British and Italian Somaliland (Fig 71) Cases have been observed clinically and confirmed by laboratory methods as far east as Kenya and the Anglo Egyptian Sudan

oriented by the occurrence of human cases were unsuccessful until 1938 when infected *Haemagogus capricornii Aedes (Finlaya) leucocelaenus* and an unidentified sabethine were captured in the forests of the State of Rio de Janerio Brazil In 1944 virus was isolated from naturally infected marmosets captured at Ilheos Bahia Brazil

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southern Brazil when there were an estimated 15 000 cases in the states of Minas Geraes and Rio de Janeiro In spite of the fact that yellow fever is undoubtedly much more prevalent in West Africa than in the Anglo Egyptian Sudan the largest recorded outbreak in Africa was that in the Nuba Mountains in 1940 with over 20 000 cases The importance of yellow fever cannot be gauged by the number of reported cases but by the threat of epidemics in pres ently clean areas

THE ETIOLOGIC AGENT

The ultramicroscopic filtrable nature of the causative agent of yellow fever was reported by Reed and Carroll in 1902 but was not fully accepted previous to 1927 when the virus was established in laboratory animals Once so established the virus of yellow fever has been studied intensively The limited geographic distribution of yellow fever with the consequent availability of definite negative controls and the high specific antigenicity of the virus have made this agent especially valuable for developing methods and technics applicable to the more general study of viruses

The virus of yellow fever is one of the smallest of the pathogenic viruses (between 17 and 28 millimicrons) When thoroughly des iccated it can be preserved over long periods at low temperatures It succumbs readily to a temperature of 55 C and is very suscep tible to chemicals and disinfectants

The inoculation of yellow fever virus from a human patient sub cutaneously into the rhesus monkey and intracerebrally into the white mouse generally produces a severe disease involving the visceral organs of the monkey and the brain of the mouse The term pantropic is used to designate this unmodified virus containing both viscerotropic and neurotropic properties

Repeated brain to brain transmission of the virus in the mouse causes a decrease in viscerotropism and an increase in neurotropism The neurotropic virus no longer causes visceral disease in the mon key but does produce encephalitis when inoculated intracerebrally It has a shortened incubation period in mice with a mortality approaching 100 per cent The neurotropic virus has been widely used in the neutralization test

Yellow fever virus has been grown in special tissues both *in vitro* and *in vivo* and has been adapted to chick embryos and even to young chicks The famous 17D strain used for vaccination since

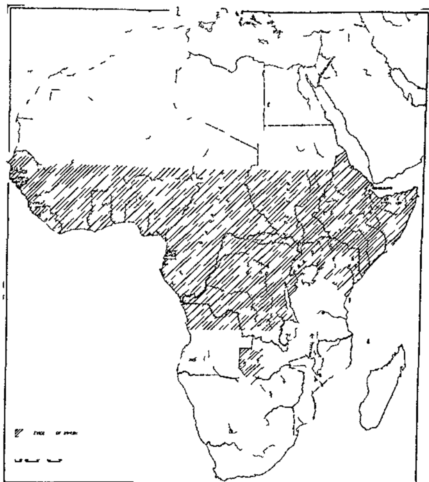


FIG 71 —Yellow Fever Areas of Africa Based on 3rd Report of the Expert Commission on Quarantine Epidemiological Information Bulletin Vol 1 No 16 September 1945

PREVALENCE

The prevalence of yellow fever is most difficult to determine and available official statistics are often misleading In the absence of *dramatic epidemics only routine viscerotomy can be expected to* reveal the presence of the disease There have been no important urban outbreaks of yellow fever in the Americas since the one occurring in Rio de Janeiro in 1928 29 and most of the jungle yellow fever occurs in rural areas many of which are isolated and without medical services That even jungle yellow fever may be an important disease in its own right is shown by the 1938 epidemic in

certain forms especially the lower primates virus may circulate for several days after a variable incubation period But the circulation of virus is always limited and never continues over long periods in the same individual nor does it recur at intervals In other forms such as the canines inoculation of virus is not followed by circulation of the virus in recoverable amounts In still other vertebrates circulation is uncertain and in small amounts Animals which circulate virus in amounts so small that insect infection does not occur can take no part in the epizootiology of the disease

The vaccine virus 17D can circulate in man and in the rhesus monkey but it has been impossible to infect mosquitoes by allowing them to feed on vaccinated vertebrates

The yellow fever virus is highly antigenic producing specific homologous antibodies in the primates and certain other forms The antibodies are long enduring and generally persist throughout life The neutralization test for yellow fever immunity is one of the most specific of all biological tests when applied to the blood of primates and certain other forms susceptible to infection with the production of immunity The blood of certain groups apparently contains virucidal substances which may give rise to doubtful tests

Complement fixing antibodies and precipitins are produced in man and monkeys in yellow fever but tests based on such production have not been widely used since the development of the neutralization test in white mice Apparently some information as to the severity of the attack and even of the remoteness of the attack might be obtained by combining such tests with the neutralization test

VERTEBRATE HOSTS

A vertebrate to be of importance in the natural maintenance of yellow fever must be (1) relatively numerous (2) susceptible to infection with circulation of large amounts of virus in the peripheral blood stream (3) acceptable and accessible to the vectors as a source of blood meals

The ideal host would be a short lived and prolific vertebrate not killed by the infection since a constant supply of non immune hosts is required to keep the infection going Man the traditional victim of yellow fever fails to fulfil these conditions and history is full of instances when yellow fever invaded an area only to die out after

1937 became modified while in tissue culture of embryonic chick cells in such a way that it is no longer viscerotropic for the rhesus monkey and has a greatly reduced neurotropism as shown by the prolonged incubation period in the mouse and the low percentage of rhesus monkeys which develop encephalitis even after direct intracerebral inoculation

Yellow fever virus has not been grown in the absence of living cells The essential intracellular nature of the virus is emphasized by the observation that the addition of immune serum to tissue culture does not destroy the virus already present in the cellular elements There is no evidence of different phases in the life cycle of the virus and the infected mosquito can be shown to have the virus in active form at all times after the infective meal The extrinsic incubation period of yellow fever apparently depends on the speed with which the virus is able to multiply within the cells of the mosquito and spread to the salivary glands

The behavior of the virus in different blood sucking invertebrates varies In some there seems to be no persistence of the virus beyond a few hours after the infective meal In others the virus persists for days and even weeks but apparently never invades the salivary glands since transmission does not occur Even among those mosquitoes which can be shown to transmit the virus there are wide variations in the ease with which transmission occurs and in the percentage of each species which becomes infective Although it is possible to produce infective adult mosquitoes from larvae immersed in high concentrations of serum virus there is no evidence that the virus ever carries over from one generation to the next

The infected insect apparently remains infected for life Virus has been observed to persist three months in a self propagating protected colony of aegypti mosquitoes But in nature yellow fever routinely disappears some 6 weeks after the effective curtailment of aegypti production in infected districts

The behavior of virus in vertebrates varies so widely that it is unsafe to draw conclusions on any form which has not been exposed to the virus under controlled conditions in the laboratory In man after an incubation period of 2 to 6 days virus is found circulating in the bloodstream in sufficient quantities to infect mosquitoes during the first 72 hours after onset of illness The more sensitive test of animal inoculation has revealed virus as late as the fifth day In





FIG 72 —Types of areas in Brazil where jungle yellow fever has occurred In the community pictured above cases were limited to workers in the fields adjoining the jungle six kilometers from the settlement In the house shown below which was situated on the edge of the jungle eleven tenants had suspicious attacks of fever within a few months and later proved immune to yellow fever

a short time in spite of an adequate density of aegypti mosquitoes Only large cities with a constant influx of non immunes could maintain the disease constantly in a small area over long periods of time Through crowding in towns and cities and through trade and immigration, man created conditions which during the 18th and 19th centuries permitted yellow fever to become the greatest scourge of the American tropics

Observations on jungle yellow fever show that the forest infection *tends to persist at a given point for a comparatively short time* generally measured in weeks or at most in months The intervals between sweeps of the virus through a given area vary widely Certain relatively small districts such as Muzo in Colombia and Ilheos in Brazil seem to keep the virus circulating with a short cycle of 1 to 3 years whereas the observed cycle in the Vale do Canaan where yellow fever without *Aedes aegypti* was first confirmed in 1932 was 8 years and in the states of Mato Grosso (1934 44) and Goyaz (1935 45) it was 10 years Since repeated observations in study areas have failed to show important differences in the density of probable vectors during epidemic and interepidemic periods the dying out of the virus is attributed to the reduction of the susceptible vertebrate population to the point where the local vectors can no longer keep the infection active

Extensive yellow fever immunity surveys of animal populations in South America and Africa have been made Among the forms found positive only the primates the marsupials and the rodents are present in sufficient numbers to be considered important as vertebrate hosts The results of laboratory infections suggest that of these the primates must be given special consideration in the epizootiology of yellow fever In certain districts where jungle yellow fever has occurred however primates are very scarce and the possibility of other hosts must be considered Marsupials some of which can be infected in series have been reported as an element in the cycle in Colombia Although some of the large rodents have been found naturally immune there is little or no evidence incriminating them in the yellow fever cycle

The observed rapidity of spread of yellow fever in southern Brazil between 1934 and 1940 suggested the intervention of more rapidly moving forms than mosquitoes and primates or marsupials Studies on a relatively small number of families of birds have failed to reveal any susceptible species

For Africa

Aedes (Stegomyia) metallicus
Aedes (Aedimorphus) stokesi
Aedes (Stegomyia) africanus
Aedes (Stegomyia) luteocephalus
Aedes (Stegomyia) simpsoni
Aedes (Stegomyia) vittatus
Aedes (Diceromyia) taylori
Eretmopodites chrysogaster
Taeniorhynchus (mansonioides) africanus
Culex thalassius

For South America

Aedes (Ochlerotatus) scapularis
Aedes (Finlaya) leucocelaenus
Aedes (Taeniorhynchus) fluviatilis
Haemagogus capricornii
Haemagogus spegazzinii

For North America

Aedes (Finlaya) triseriatus
Aedes (Taeniorhynchus) taeniorhynchus

For Europe

Aedes geniculatus

For East Indies

Aedes (Stegomyia) albopictus

Of these *Haemagogus capricornii Haemagogus spegazzinii* and *Aedes leucocelaenus* in America and *Aedes simpsonsi* and probably *Aedes africanus* in Africa have been found infected in nature

The first evidence that *Haemagogus* might be involved in the transmission of jungle yellow fever came in 1935 from the State of Goiaz Brazil after laboratory tests with this genus had given dis appointing results The natives of districts where yellow fever oc curred insisted and observation confirmed that the principal blood sucking insects which molested them as they worked at the edge of the forest was the "little blue mosquito" Three years later *Haemagogus capricornii* together with *Aedes leucocelaenus* and an

INVERTEBRATE VECTORS

An arthropod to be of importance in the maintenance of yellow fever must be infectible sufficiently long lived to survive the extrinsic incubation period numerous and widespread and must feed on susceptible vertebrates

The *Aedes (Stegomyia) aegypti* mosquito is probably the only arthropod capable of maintaining yellow fever for long periods as a human disease This vector adaptable as it is to completing its life cycle on shipboard must have been responsible for the trans Atlantic passage of the yellow fever virus

Aegypti has occupied its position as the yellow fever mosquito not because it is more infectible or transmits the virus more readily *than certain other mosquitoes but rather because of its adaptation* to the completion of its life cycle in close contact with man in and around human habitations Thoroughly adapted to passing through the aquatic stages in clean water in containers such as jars tanks, barrels tins roof gutters cisterns cocoanut shells etc and having a resistant egg viable for many months when properly matured aegypti has spread from its Old World home around the globe with man The tropical forests of the Americas are free of the aegypti mosquito but those of Africa harbor it in small numbers Aegypti control measures in the Americas are generally required only in and about human habitations Aegypti is often most dangerous in regions where there is so little water at certain seasons of the year that supplies have to be conserved by storing and it has never effectively established itself in many small centers of population along the Amazon where water is so constantly accessible that no storage occurs

Aegypti requires about a week under ideal conditions to develop from egg to imago If an aegypti feeds on a vertebrate in whose blood stream the virus of yellow fever is circulating freely it can later after an incubation period in which the virus multiplies in its body transmit the infection to a non immune vertebrate by bite At the usual summer temperature the incubation period of the virus in the mosquito is 9 to 12 days Experimentally this period can be varied by keeping the infected insect at different temperatures from 4 days at 37°C to 18 days at 21

Laboratory tests have shown that many mosquitoes other than aegypti can transmit yellow fever virus from animal to animal The potential vectors include species of several different genera

those of the first period The change generally comes from the third to the fifth day The active congestion is replaced by venous congestion with low arterial tension The bradycardia may be extreme and persist in spite of a secondary rise in temperature Nausea and vomiting become more severe are associated with marked epigastric pain and are of grave import

Albuminuria is one of the most constant findings of the second period even in mild cases A sudden *progressive increase* in the albumin content of the urine in a much greater amount than can be explained on the basis of the febrile condition occurring as early as the second day or as late as the fourth or fifth day is almost pathognomonic of yellow fever

Overwhelming intoxication becomes apparent with the appearance of the dreaded triad—jaundice hemorrhage and anuria

Hemorrhage may be slight or severe and jaundice is generally slight during the first four or five days of illness But some degree of icterus and some tendency to hemorrhage can be found in practically all clinically diagnosable cases Although hemorrhage black vomit and melena never fail to impress the patient and the lay observer the most dreaded symptom for the experienced is anuria Anuria seems to depend on the destruction of liver parenchyma and its appearance is not closely correlated with that of albuminuria

Death may occur as early as the second day but is more common from the fourth to the seventh days Although late deaths do occur the disease has generally run its course before the tenth day Late deaths are generally due to intercurrent infections

The observation of previous generations of clinicians that numerous mild immunizing infections occur during epidemics of yellow fever has been amply confirmed by the isolation of virus and by immunity surveys before and after known outbreaks Mortality figures for different outbreaks and different areas vary but *clinically diagnosable* yellow fever is always a serious disease carrying a mortality ranging from 40 per cent upward Yellow fever infection on the other hand probably has a mortality of somewhere between 5 and 10 per cent

The differential diagnosis of yellow fever is not difficult when several associated cases with adequate histories can be examined The clinical diagnosis of a single case on first inspection may be most confusing since various severe infections and intoxications in

unidentified sabethine was found naturally infected in the forests of Rio de Janeiro, Brazil In Colombia in 1940 and 1941 natural infections were found in *A leucocelaenus* and in mosquitoes then identified as *H capricornii* Recently evidence has been presented to show that the most important mosquito vector of yellow fever in Colombia previously identified as *H capricornii* Lutz is really a subspecies of *H spegazzinii* Brethes known as *H spegazzinii falco*

The accidental observation by Boshell that *Haemagogus* prefers to live considerably above ground level has led to studies in both America and Africa which indicate that jungle yellow fever is largely arboreal This finding helps to explain the high incidence of jungle yellow fever among wood cutters and lumbermen and among farmers at the time new fields are being cleared

YELLOW FEVER IN MAN

The symptoms of yellow fever are those of an acute infection—fever headache backache, congestion pain in the legs vomiting and severe prostration—followed on the third day by those of a severe intoxication associated with disturbances of renal and hepatic function These symptoms of intoxication are common to a number of diseases and intoxications involving destruction of liver parenchyma The classical clinical picture of yellow fever depends not so much on the symptom complex—hemorrhage jaundice albuminuria and anuria—as on the timing and sequence of their appearance with relation to onset In yellow fever the onset is usually abrupt after an incubation period of 2 to 6 days and both pulse and temperature tend to reach their peaks within a few hours after onset Both drop on the second and third days the pulse earlier and more rapidly than the temperature (Faget s sign) The pulse may be expected to be below 100 by the third day and to drop to the fifties or even forties as the disease progresses Initial headache and facial congestion are constant findings Although epistaxis localized hemorrhages low albuminuria and slight jaundice may be apparent during the first days of illness the classical symptoms of yellow fever appear characteristically during the period of intoxication

The periods of infection and intoxication may be separated by a spurious lull in which the patient has a sense of well being but often one period shades into the other In fulminant cases the symptoms of infection are precocious and may blend early with

The greatest concentration of necrotic cells is in the midzone of the lobule and the necrosis of the cells about the periphery and the central vein is never complete

TREATMENT

No specific therapy of value has been found for yellow fever Chemical analyses of the blood suggest the use of glucose to combat hypoglycemia and of calcium salts to neutralize the guanadine like toxins common to destruction of liver parenchyma but these measures have not been followed by recovery in monkeys showing signs of intoxication nor have striking results in man been demonstrated Vitamin K has been suggested but no data are available as to its value

All cases of yellow fever infection merit careful handling which means handling as little as possible Unless unavoidable the patient *should not be moved from the place of onset of the disease* after the first day Activity during convalescence should be renewed gradually

The gastro intestinal tract should be relieved by a saline purge on the first day Abstinence from food except fruit juices is recommended during the initial period and until the temperature returns to normal in the intoxication phase

For relief of vomiting cracked ice and codeine hydrochloride may be given by mouth Antipyretics are contraindicated

EPIDEMIOLOGY

Aegypti transmitted yellow fever in the Americas tends to attack both sexes and all ages and races when first introduced into a community In towns where the disease has previously occurred the distribution of cases will depend on the distribution of immunity from previous outbreaks In highly endemic areas infection is limited to the young age groups Since the human population is slow to replace one generation with another the continued presence of yellow fever as a strictly human disease in a region depends on (1) large population centers where the number of non immune arrivals from births and immigration is great and (2) large rural and village populations together with a widespread distribution of the aegypti mosquito able to maintain a wandering endemicity Human yellow fever tends to die out through failure of the human host in towns and villages subject to explosive outbreaks of yellow fever

volving the liver parenchyma may produce albuminuria hemorrhage jaundice and anuria Fortunately the laboratory can help through

1 Isolation of virus by inoculation of the rhesus monkey or white mouse with blood from a person suspected of having yellow fever
2 Neutralization test during the first three days of illness repeated after the fifth day If the first test is negative and the second positive the presence of yellow fever is definitely confirmed If both are negative or if both are positive yellow fever can be ruled out A single positive test on the fourth day or later is inconclusive *since the date of infection cannot be fixed*
3 Microscopic examination of liver tissue removed post mortem The pathologic picture in the liver is very characteristic and for practical purposes is almost pathognomonic Certain intoxications (carbon tetrachloride tannic acid) may cause confusion in individual cases in which details of the clinical picture are unknown but no other acute infectious disease has been found to duplicate the yellow fever lesion

PATHOLOGY OF YELLOW FEVER IN MAN

On post mortem examination the heart is apt to be found pale and flabby the kidneys tense and swollen Hemorrhage may be seen in any of the organs or serous surfaces but is especially common in the stomach and intestines where partially digested blood is often observed

From the standpoint of differential diagnosis the liver is the all *important organ to be examined In yellow fever it is generally* normal in size and of a mottled color and a fatty consistency The gross appearance often fails to indicate the degree of destruction to be found on microscopical examination

On microscopic section the typical yellow fever liver shows fatty degeneration and a widely varying amount of parenchymal necrosis without evidence of inflammation or of connective tissue proliferation There is a *jumbling of the trabeculae which is more accentu*ated in the midzone of the lobule The number and size of the fat globules observed vary greatly The necrosis of the parenchyma *may* involve a few or almost all of the cells but its distribution is always of a "salt and pepper" rather than of a focal or massive type

Man is not an essential factor in the mechanism of jungle yellow fever transmission and often takes no part in maintaining the virus since if acutely ill he remains at home The distribution of immunity in the human population cannot be taken as a measure of the immunity of the susceptible animals in the forests Jungle yellow fever tends to spread entirely independently of human travel routes In general it makes its way through forest areas and along gallery forests bordering streams but it also appears in isolated bits of forest which have no connection with the main source of infection It is difficult to reconcile the observed spread of the disease with what is known of the rate of travel of vertebrate hosts and the dissemination of known invertebrate vectors

Cases of jungle yellow fever have been observed to initiate aegypti transmitted outbreaks in a number of instances in South America during the past decade and it is probable that the virus causing the outbreak in the Anglo Egyptian Sudan in 1940 was of recent jungle origin

PROPHYLAXIS OF YELLOW FEVER

In these days of rapid travel all parts of the world suitable for yellow fever are accessible from known infected areas within the incubation period of the disease in man The control of yellow fever then is important not only to South America and Africa but also to those countries where conditions exist which would permit outbreaks were the virus introduced The United States Mexico Central America the West Indies all have an interest in yellow fever in South America India Asia and Australia where yellow fever has never been known are vitally interested in yellow fever in Africa since they have all the elements except the virus for the production of a holocaust Once introduced into Asia yellow fever might well become established as an urban and jungle disease

The discovery of jungle yellow fever first in Brazil and later in several other countries of South America and Africa the demonstration that this jungle yellow fever in animals constitutes a permanent source of virus for the infection of clean areas the proof that the jungle yellow fever regions of Africa extend practically across the continent from the Atlantic to the Indian Ocean and the development of rapid interregional aviation with its inherent threat of carrying passengers in the incubation period of infection from endemic to clean areas have all stimulated among health workers a

Aegypti transmitted yellow fever tends to spread slowly within the infected community and its movement from one place to another is along the lines of human travel In the past yellow fever has spread through transport of the infected vector through transport of the infected human during the incubation period of the disease or during the early days of illness and also through the transportation of all the elements of an epidemic—infected humans infected mosquitoes, non immunes and a breeding colony of aegypti on shipboard Under modern conditions the greatest threat of long distance transportation of yellow fever virus to clean areas is the air passenger traveling during the incubation period of the disease

Jungle yellow fever apparently depends on a supply of non immune animals in the forest and tends to die out rapidly in many places within a matter of weeks after discovery In other outbreaks the virus persists much longer the whole picture being remarkably similar to that observed for human yellow fever The entire epizootic period for given areas has been observed to vary widely from 3 to 10 years probably depending on the rapidity with which a large non immune population of susceptible animals could be established and on the intimacy of contact with areas where the virus was present at the time the non immune population became established Much of our knowledge of jungle yellow fever in the past has come from investigation of outbreaks in humans It is now apparent that jungle yellow fever tends to be arboreal rather than terrestrial and that animal infections may pass through a district without the production of human cases Field studies indicate that in the jungle just as in the cities and towns yellow fever virus lives a wandering existence passing constantly from place to place even in the most suitable areas

The distribution of human cases of jungle yellow fever will depend in great part on local conditions and even on local industries Among Indian tribes living in the forest all ages and both sexes are apt to become infected early in life and the distribution of immunity resembles that seen in urban populations subject to the aegypti transmitted disease In other districts where the young boys and girls work in the coffee plantations bordering the infested forest cases tend to occur in young men and in boys and girls In still other districts where heavy logging is going on women and children are of little use and cases are found to be limited to adult men

tion eradication of adult aegypti should be much easier than heretofore and a return to the combined attack on the adult and larval forms is anticipated

VACCINATION

Vaccination with modified yellow fever virus began as early as 1931 but only since 1937 has it been practiced on a large scale The 17D virus now used in vaccination is apparently free of all tendency toward viscerotropism and possesses a greatly reduced neurotropism Millions have been vaccinated with this virus and in spite of certain difficulties which have been encountered from time to time it can be considered as one of the most successful immunizing agents known Inoculation may be followed by slight symptoms of malaise 5 to 7 days later but in general persons immunized with this virus feel nothing Neutralization tests show that most of those inoculated develop demonstrable antibodies and field observations indicate that adequate protection develops in most cases within a week Vaccination is recommended for all persons living in or traveling to or through tropical areas of South America and Africa and then proceeding to other parts of the world It is of primary importance to inhabitants of forest areas since there is not now any known method of preventing jungle yellow fever except through vaccination Vaccination apparently gives a long lasting immunity and it is probable that the period of 4 years now officially designated as the proper interval between vaccinations will be lengthened

Vaccination has a great advantage over antilarval measures as a means of controlling yellow fever in that its protective action begins much earlier than does that of the curtailment of mosquito breeding Vaccination in mass of the entire population together with the rapid spraying of all houses with DDT should be the first line emergency measure against urban yellow fever

Since it is the human case which represents the principal threat of the spread of the virus from the jungle to the town or rural settlement infested with mosquitoes capable of effective transmission of the human disease and since it is the human case which endangers clean regions the vaccination of native populations in rural endemic regions may be expected not only to reduce the incidence of jungle yellow fever but indirectly to reduce all yellow fever in the future

renewed interest in yellow fever control Fortunately the recognition of the increased threat comes at a time when control methods are vastly superior to those of 15 years ago The development of an efficient vaccine providing a means of individual protection and the improvement of methods for the eradication of *Aedes aegypti* permit the health worker to face the future with equanimity



FIG 73 —The water containers in the court yard of this Brazilian home are being inspected by a member of the yellow fever staff *for evidences of mosquito breeding*

ANTI AEGYPTI MEASURES

In the early years of this century anti aegypti measures consisted of fumigation of houses to destroy the adult mosquitoes and of weekly inspections of all premises to prevent aegypti breeding in neglected exposed water in various types of artificial containers Both measures proved to be very expensive and fumigation was eventually abandoned following the observation that antibreeding measures alone would cause the disappearance of yellow fever in about the same period as the combined program In recent years antibreeding measures have been so improved that complete species eradication is now standard practice for anti aegypti campaigns [1] *After eradication a small survey squad carrying out inspections at long intervals is sufficient to guard against dangerous reinfestation thus making permanent control possible at low cost* Brazil and Bolivia have led the way in promoting *regional eradication of the aegypti mosquito This measure* is very important in preventing the spread of yellow fever away from the jungle area *and is also valuable for the control of dengue* With the development of the DDT insecticide with its residual toxic ac

[1] See The Organization of Permanent Nation wide Anti *Aedes aegypti* Measures in Brazil by F L Soper D Bruce Wilson Servulo Lima and Waldemar Sá Antunes New York 1943 *The Rockefeller Foundation*

6 The disease may be introduced into towns and cities resulting in large epidemics
7 Jungle yellow fever occurs in extensive areas of South America and Africa
8 Rapid means of communication has increased the possibility of spreading the disease to other parts of the world
9 An efficient vaccine is available for the protection of man

QUARANTINE AND TRAVEL RESTRICTIONS

The attempt to delimit dangerous yellow fever areas for the purpose of establishing quarantine and travel restrictions encounters difficulties and these difficulties should increase rather than decrease with the widespread use of vaccination Vaccination will prevent the human cases which have heretofore been an indication of the existence of yellow fever in the jungle and will make the neutralization test unreliable since this test does not differentiate between the immunity produced by an attack of yellow fever and that produced by vaccination More and more will it be necessary *to rely on immunity surveys in animals to follow the movement of* yellow fever virus in the forests

In considering the results of immunity surveys it must be remembered that a highly immune population may be innocuous for the immediate future whereas one with a low index may be on the eve of becoming dangerous The region in which yellow fever has previously been present but in which no evidence of its recent existence can be found may be just awaiting the chance introduction of the virus from contiguous areas to become active Thus the forest areas of southern Brazil were invaded by a wavelike epizootic between 1934 and 1940 But the disease died out in each forest soon after it appeared and careful investigations failed to reveal cases in the following years But in 1944 cases were once more diagnosed in the area first found infected in 1934 and the area of the 1935 epidemic produced numerous cases in 1945 It would seem best to consider all areas in which jungle yellow fever has once been found and all *areas in which immune primates have been captured as potentially* dangerous In the same way all cities and ports in close proximity to such areas should be considered dangerous if infested with aegypti

ITEMS OF NOTE

1 Yellow fever is a disease of man and animals
2 It is caused by a filtrable virus
3 In the jungle primates and marsupials seem to be reservoirs of infection although other animals may be implicated
4 The vectors of the disease are *Aedes* and *Haemagogus* mosquitoes
5 *Persons* living in the forest or working in areas adjacent to the forest are liable to become infected

tinct from choriomeningitis The discoverers designated this virus pseudo lymphocytic choriomeningitis Other viruses have been described from time to time which occasionally produce a lympho cytic meningitis in man and which might be clinically confused with lymphocytic choriomeningitis such as La maladie des Proch ers herpes febrilis etc

Lymphocytic choriomeningitis virus passes through V N & W Berkfeld (26) Chamberlin L (3 27) and Seitz filters The more reliable estimates of the size of the virus particles vary from 35 to 60 millimicrons (28 29) The virus multiplies in the chick embryo (30) It is readily preserved in buffered glycerine at a temperature of 3 C or when rapidly frozen or in the dried state at low tempera tures Saline is deleterious to the virus

ANIMALS SUSCEPTIBLE

Many species of animals have been found capable of being ex perimentally infected by the virus including man (31) chimpan zees (31) several types of monkeys guinea pigs and white rats (2 26) cotton rats (32) rice rats (32) white mice (2) gray mice (3) dogs (6 47) baby pigs (33) and fitches (9) In rabbits (33) young chickens (33) syrian hamsters (34) ground squirrels (35) mule deer (35) and horses (35) the virus produces very slight or no recognizable symptoms but virus has been recovered from the blood or organs after varying numbers of days

Cattle and calves (33) canaries and hedge hogs (35) have been tested and are apparently insusceptible to the virus

SYMPTOMATOLOGY

Choriomeningitis may produce markedly varying symptoms in different individuals depending upon the severity of the attack and upon the localization of the virus Several clinical types of the disease have been recognized

(1) *Grippal or Non nervous Type* Cases characterized by fever malaise prostration lumbar pains and leucopenia following experi mentally induced infections have been noted by French observers (31) and in this country spontaneously acquired cases have been recognized in laboratory workers (40 41) Recovery after a week or ten days may terminate the illness or may be followed by symp toms of central nervous system involvement

(2) *Meningeal Type* Meningeal symptoms may initiate the at

CHAPTER XXX

LYMPHOCYTIC CHORIOMENINGITIS*

LYMPHOCYTIC CHORIOMENINGITIS is a rarely fatal acute infectious disease occasioned by a specific virus described by Armstrong and Lillie in 1934 (1)

The virus which in man produces varied clinical manifestations has been found occurring spontaneously in white mice (2 45 21 23) house mice (3 17) monkeys (4) dogs (6) guinea pigs (7) roaches (8) and possibly ticks (9)

HISTORY

The virus of lymphocytic choriomeningitis was first isolated and described at the National Institute of Health in 1934 (1) during study of the brain from a patient who had suffered a fatal attack presumably of encephalitis (St Louis type) The virus was later isolated from the spinal fluid of a laboratory worker by Scott and Rivers (10) 1935 and has subsequently been found in widely separated regions of the United States (1 2 3 4 6 10 11 12 13 14 15 16 17 etc) Canada (9 18) England (19 20) France (21 22) Japan (23) North Africa (24)

THE ETIOLOGIC AGENT

While there is evidence that strains of choriomeningitis virus from different sources may vary somewhat in their virulence for experimental animals and in their affinity for various organs they have with few exceptions been immunologically similar McCallum Findley and Scott (25) isolated a virus from two cases of illness clinically resembling choriomeningitis When the virus was inoculated into monkeys and mice the pathologic lesions simulated those of choriomeningitis but immunologically the virus seemed to be dis

* Prepared by Charles Armstrong M D Medical Director United States Public Health Service

Choriomeningitis is most often confused with tuberculous meningitis or with acute aseptic meningitis of unknown etiology but must be differentiated from syphilitic meningitis torula hystolitica meningitis poliomyelitis mumps menigo encephalitis post infectious encephalitis and herpes meningitis as well as other types of meningitis and encephalitis The grippal type of cases so far identified was indistinguishable clinically from uncomplicated influenza

PROGNOSIS

Recovery is usually complete in from two to three weeks but one or more relapses are not uncommon and recovery has in some instances been delayed for several weeks to even months Moreover permanent ill effects related to disturbances of the cerebrospinal drainage have resulted in some cases for instance Barker and Ford s (11) patient suffered from permanent symptoms which led to the performance of a laminectomy the subarachnoid space was found to be obliterated by fibrous tissue A group of three exceptionally severe related cases all of which terminated fatally is mentioned below

SOURCES OF INFECTION

With the exception of one case contracted through exposure at an autopsy there is no history among proven cases suggesting that the infection was in any instance acquired through contact with another case The lack of evidence of spread from patient to patient together with the finding of the virus in uninoculated white mice (2 45 21 23) gray mice (3 17) monkeys (4 5) dogs (6) guinea pigs (7) and possibly ticks (9) naturally suggests the existence of some animal reservoir for the virus from which man becomes infected Workers from the National Institute of Health (3 46) investigated the homes of several patients to determine the presence of arthropods mice rats pets etc which might possibly have served as the reservoirs for the infection Only gray mice were found common to the houses investigated Gray mice were trapped in each abode and choriomeningitis virus was isolated from emulsions of liver and spleen of mice trapped in five of the six homes investigated The single failure was in a home previously overrun with mice and the patient prior to illness had recently trapped twelve in his pantry and had disposed of them with

tack or may follow the grippe like symptoms often after a more or less complete remission of symptoms of several days duration Fever severe headache vomiting stiff neck positive Kernig and Brudzinski signs are usual

(3) *Meningo encephalitic Type* In addition to such meningeal symptoms as have been described above, somnolence anaesthesia paralysis, and impaired vision pointing toward involvement of the brain or cord may occur

(4) *Asymptomatic Type* Among 2000 sera examined at the National Institute of Health by means of the serum virus neutralization test between 12 and 13 per cent gave reactions indicating immunity A considerable sample of these immune individuals were investigated and a history suggesting an attack of choriomeningitis or any central nervous system involvement was the extreme exception Nearly all the individuals however gave a history of grippe like illness which may or may not have been choriomeningitis In view of the varying severity of proven cases it seems probable that attacks producing immunity but no symptoms may occur Such have not however been actually recognized

LABORATORY DIAGNOSIS

In central nervous system types of the infection the spinal fluid is clear sterile to culture sugar content is usually within normal limits and the cell count may reach 3200 the cells being mainly lymphocytes The virus may be recovered from the spinal fluid or blood especially in the early days of the disease through the intraperitoneal inoculation of guinea pigs or the intracerebral inoculation of mice Guinea pigs are preferable for primary isolation Specific virus neutralizing or complement fixing antibodies may be demonstrated following an attack Neutralizing antibodies however are usually not demonstrable prior to 6 weeks following onset but may persist for years Complement fixing antibodies appear earlier but are of short duration (57 58 59)

DIFFERENTIAL DIAGNOSIS

An etiologic diagnosis is largely the concern of the laboratory and may be established either by transmitting the disease to guinea pigs or mice or by demonstrating the development of specific antibodies in the serum following recovery

weaken or disappear Haas (51) moreover demonstrated that congenitally infected mice were far more efficient transmitters of the disease to cage mates than were mice experimentally inoculated after birth

Mice an Effective Reservoir—The occurrence of cases of choriomeningitis as well as protective antibodies among persons in the lower economic strata of society is consistent with the concept that mice are a source of human infection

The fact that mice were abundant in the houses of all of six cases studied in Washington and that virus was recovered from mice caught in five of the six abodes points in the same direction A certain amount of direct evidence bearing on this point is afforded by the development of choriomeningitis among investigators who have contracted the disease while handling infected mice in the laboratory (40) or by patients who have had direct or indirect contact with gray mice prior to illness (17 53 47 19)

Reservoirs of Infection other than Mice—The virus has several times been isolated from the tissues of dogs during investigation of canine distemper (6 7) A remarkable group of three related cases of choriomeningitis of unusual severity occurred among canine vaccine workers from each of which we succeeded in isolating the virus (47) These laboratory findings were confirmed in each case by other investigators The attacks proved fatal in all three patients thus suggesting a strain of unusual virulence The strains were all similar but peculiar in that they produced a febrile illness in rabbits and white rats which animals responded to inoculation with our original strains by the development of antibodies but without definite symptoms A young dog inoculated with this virus developed fever with marked paresis and incoordination of the hind legs but eventually recovered our earlier strains of mouse origin were inoculated into three dogs but produced no definite symptoms

The virus was possibly isolated from ticks in one instance (9) (*Dersmacentor andersoni*) and the latter have been experimentally infected by allowing them to feed upon infected animals Ticks have been proved to transmit the virus through the entire life cycle and to convey the disease to normal guinea pigs when infected nymphs were placed in their cages (52) *Aedes aegypti* mosquitoes were also shown to be capable of transmitting the disease to a guinea pig when allowed to bite five days after feeding on infected animals (15)

his own hands Extensive trapping was carried out in this home by Armstrong but only two mice were caught both of which were negative for virus

Virus among Mice Trapped in Washington D C—Armstrong (47 53) trapped over 400 live mice from 78 scattered houses in Washington D C of which 369 survived to examination From the spleens and livers of 307 of these mice 65 strains of choriomeningitis virus were isolated that is one mouse out of every 5 examined was a carrier of potent virus

These 65 infected mice came from 35 of 78 houses where mice were trapped that is 45 per cent of the mouse infected homes where trapping was carried out were harboring infected mice A total of 123 mice were caught in these 35 houses from which the 65 infected mice came i e 52 51 per cent of the mice taken in homes where infected mice occurred were harboring the virus

Sixty two gray mice from homes where infected mice had been trapped and 47 mice from homes where only normal mice had been caught were inoculated intracerebrally with 10 to 15 minimal lethal doses of choriomeningitis virus 66 per cent of the former group survived and 10 6 per cent of the latter while none of a group of 12 control mice lived These findings indicate a high proportion of immune mice among those trapped from homes harboring infected mice as compared to the controls

These findings have been confirmed by Farmer and Janeway (17) and Yamarat (48) who trapped mice in a home in which a case of choriomeningitis had occurred in Boston Virus was recovered from 5 of 10 mice taken Among a total of 108 mice trapped in Boston they found only 8 or 7 4 per cent which were carriers of the virus as compared to Armstrong s findings of 21 5 per cent for Washington D C

Source of the Infection in Mice—Mice experimentally inoculated with a non fatal dose of virus develop immunity after about 10 days (49) and rapidly free themselves of demonstrable virus When a pregnant mouse is inoculated with choriomeningitis virus however the infection passes to the unborn young which after birth develop quite normally but continue to carry the virus as long as they live and the females in turn pass the virus to their offspring At the National Institute of Health a strain of virus was observed to pass in an unbroken series from an infected mother through fifteen generations of her offspring with no apparent tendency of the virus to

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Experimental transmission from monkey to monkey by means of monkey lice was twice accomplished (47)

MODE OF TRANSMISSION

There is a striking lack of evidence to suggest person to person transmission but a close association between human cases and infected house mice has been repeatedly noted

Infection via the respiratory tract is suggested by the common early respiratory symptoms Other possible routes are the gastrointestinal tract by eating of contaminated food or through the skin (54) or conjunctiva (22) Transmission by blood sucking insects has been demonstrated in the laboratory but the fact that cases occur mainly during the colder months of the year rather than in the summer (55) indicates that they are probably of little significance in the natural transmission of the disease in the United States

INCUBATION PERIOD

Lepine and Sautter (22) cite the case of a laboratory worker who splashed infected material into her eye on March 29 1938 Classical symptoms of la grippe developed ten days later while meningeal symptoms headache and stiff neck appeared on the 19th day following the accident Farmer and Janeway's patient (17) handled a *gray mouse trapped in a house later proved to harbor infected mice* She developed fever on the 13th day and meningeal symptoms on the 21st day One of the three fatal cases which we have mentioned (47) developed systemic symptoms eight days after assisting with the autopsy of a proven case

Hays and Hartman's patient (42) exploded a tube containing virus and the material spattered into his face The patient was wearing a mask and gloves at the time but no glasses The material got into his hair and may have gone into his eyes also Fever cough and muscle soreness developed on the 16th day following the accident Blood drawn on the 19th day contained the virus

The limited evidence available suggests that the interval from exposure to onset of grippe like symptoms may vary from 8 to 16 days *while meningeal symptoms if they develop occur later* 19 and 21 days in the cases cited

PATHOLOGY

The pathology in man is not completely known since but few proven cases have come to autopsy The three deaths originating in

a laboratory where dog distemper vaccine was prepared (47) showed cerebral oedema and congestion but very little in the way of meningeal or choroid plexus involvement On the other hand blood vessel changes were evidenced by the presence of a skin rash in one and possibly in two of the cases and of focal hemorrhages in two cases These hemorrhages were found beneath the dura in the lungs the kidneys and walls of the small and large intestines The presence of free pleural and peritoneal fluid in at least two of the cases also points toward vascular injury While the strains of virus from these cases were being studied at the National Institute of Health three spontaneous infections developed among monkeys one of these monkeys developed a pronounced macular eruption which faded after three or four days The lungs in this animal were studded with hemorrhages and there was a virus rich fluid in both chest and abdominal cavities There was some congestion and oedema of the brain but the most striking lesion reported by Dr R D Lillie was a marked destruction of liver tissue beyond anything previously encountered with any of the mouse strains which we had studied It appears therefore that the strains in question which probably originated in dogs were exceptional in their virulence for man as well as in their host range and in the organ affinities Excellent pathological studies of the disease in experimental animals have been published by various authors (1 26 35 55 21 56)

PREVENTION

There is much to be determined relative to the exact method by which man becomes infected It does however appear certain that prevention would be furthered by the construction of homes with a view of rendering them mouse proof and by reducing or eliminating mouse infestation from quarters frequented by man

TREATMENT

There is no specific treatment of proven value Sulfapyridine and prontosil are of little or no value Spinal tap for the reduction of increased pressure often relieves the severe headache Patients should not be permitted to leave their beds too early owing to the tendency of the disease to relapse A good rule is to restrict the patient until the spinal fluid cell count has returned to normal limits

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ITEMS OF NOTE

1 Lymphocytic choriomeningitis is caused by a filtrable virus
2 The virus is found in mice dogs and other animals
3 The method of transmission is uncertain
4 There is no indication that the disease is transmitted from person to person
5 Methods of prevention have not been determined but elimination of mice from houses would seem to be indicated
6 There is no specific treatment

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SECTION THREE

HUMAN DISEASES SPREAD BY ANIMALS

CHAPTER XXXI

THE RELATION OF HUMAN INFECTIONS TO ANIMALS

THERE are eighty three communicable diseases listed by the American Public Health Association which are of public health significance (1) More than half of this number find no reservoir in animals nor do animals have any part in disseminating the causative agents They are as follows

Bartonellosis
Chancroid
Chickenpox
Cholera
Common cold
Conjunctivitis acute infectious
Dengue
Diarrhea of the new born epidemic
Dysentery bacillary
Encephalitis type A (Vienna type)
Filariasis
Food poisoning Staphylococcus
German measles
Gonorrhea
Granuloma inguinale
Hepatitis infectious (acute catarrhal jaundice)
Hookworm disease (ancylostomiasis
Impetigo contagiosa
Influenza
Kerato–conjunctivitis infectious
Leishmaniasis American
Leprosy
Lymphogranuloma venereum (inguinale)
Malaria
Measles
Meningococcus meningitis
Mononucleosis infectious
Mumps
Paratyphoid fever (paratyphoid A)
Pediculosis
Pemphigus neonatorum
Pertussis
Pneumonia pneumococcal
Pneumonia bacterial other than pneumococcal
Poliomyelitis

Relapsing fever louse borne (epidemic)	Syphilis
Rheumatic fever	Trachoma
Sandfly fever	Typhoid fever
Scabies	Typhus fever louse borne (epidemic)
Streptococcal infection—erysipelas	Vulvovaginitis in children
Streptococcal infection—puerperal fever	Yaws
	Yellow fever—epidemic

Epidemiologic evidence from time to time seemed to implicate animals in the spread of some of these infections Poliomyelitis has been associated with dogs cats chickens and colts in various reports Hull investigated an epidemic of paralysis among hogs on a farm where two children were sick with poliomyelitis but histologic examination of the spinal cord of the hogs revealed no evidence to indicate that the affection was poliomyelitis Two colts on another farm where poliomyelitis existed in the family were kept under observation for several weeks but the so called paralysis apparently was due to a nutritional deficiency Frost (2) investigated the connection of paralyzed dogs chickens and rabbits to the epidemics of poliomyelitis in Iowa in 1910 and in Cincinnati Ohio in 1911 finding no evidence to support the contention that such animals were suffering from the disease or acting as carriers Rillo and Lagrotta in Argentina have drawn attention to the domestic fowl as a reservoir of poliomyelitis virus It is suggested that the vector of transmission is the chicken louse *Dysmanisium avis* The work has not been confirmed (11)

Jungeblut and Dalldorf (3) encountered three house mice from which they isolated a virus similar to that of poliomyelitis but greatly attenuated The mice were taken from a house in which a fatal case of the disease had occurred Pearson (4) isolated a virus from twenty two Norwegian rats on a city dump that caused paralysis in mice and cotton rats

Work done at the University of Berne Switzerland would indicate the cow and the hog as reservoirs of poliomyelitis infection One case of spontaneous poliomyelitis in a heifer was reported from Berne (6) in which the microscopic findings were typical of the disease Poliomyelitis has been transmitted through cows milk in the United States but it was not believed that the cow had any connec

tion with the contamination of the milk It is probable that animals have a small part if any in the epidemiology of poliomyelitis

Typhoid fever transmitted by the hen through the egg has been suggested as a possibility It is known that poultry will readily partake of human feces if given the opportunity and this happens on occasions too numerous around poorly protected privies and outhouses Mitchell and Bloomer (5) however found hens entirely refractory to the typhoid bacillus both by injection and ingestion nor was a carrier" state set up There is no evidence to believe that the hen is capable of transmitting typhoid through the egg

Typhoid fever is often transmitted through cows milk but the cow is not responsible even though she partakes of badly infected drinking water Contamination of the milk in every instance arises directly from a human source

Influenza of human origin has been suspected of causing influenza in hogs which first appeared in 1918 Laidlaw (7) attempted to show that swine influenza was an altered form of human influenza the original infection occurring during the 1918 epidemic Shope (8) demonstrated that antibodies capable of neutralizing the virus of human influenza were present in the blood serums of old swine on two New Jersey farms but absent from the serums of young swine on the same farms The possibility of the dissemination of the virus by earthworms which ingest swine lungworms from infected hogs and are later themselves devoured by other hogs has been suggested It has now been shown that the virus of swine influenza is distinct from the virus causing human influenza

Paratyphoid fever is an enteric infection caused by *Salmonella paratyphi A* or *S paratyphi B* Paratyphoid A is practically never found in animals Paratyphoid B has been encountered in fowls on four occasions and other animals a few times Animals play such a small part in the epidemiology of the disease however that they can be ignored for all practical purposes

ANIMAL DISEASES OF PUBLIC HEALTH SIGNIFICANCE

There are thirty diseases listed by the American Public Health Association that may be derived from animals Twenty four of these are primarily animal in origin Man is subject to infection usually directly from an animal and rarely passes the infection on to another person Isolated instances can be enumerated however where some of the diseases have been passed from person to person In the pneu

monic form of plague such direct contact is the usual form of dissemination Tuberculosis other than pulmonary includes the bovine and avian types but may also include the human type

- Actinomycosis
- Anthrax
- Boutonneuse fever
- Brucellosis (undulant fever)
- Choriomeningitis lymphocytic
- Encephalitis epidemic (St Louis type)
- Encephalomyelitis equine
- Food Infections (salmonellosis)
- Glanders
- Haverhill fever
- Hemorrhagic jaundice (leptospirosis)
- Plague
- Psittacosis
- Q fever
- Rabies
- Rat bite fever
- Relapsing fever tick borne (endemic)
- Rocky Mountain spotted fever (tick typhus)
- Trichinosis
- Trypanosomiasis American
- Tsutsugamushi disease (mite typhus)
- Tuberculosis other than pulmonary
- Tularemia
- Typhus fever endemic (flea borne typhus)

Several diseases of public health significance are sometimes associated with animals but may be transmitted in various other ways

- Coccidioidomycosis (coccidioidal granuloma)
- Dysentery amebic
- Favus
- Ringworm
- Yellow fever jungle

Botulism tetanus and gas gangrene are infections which cannot be charged directly to animals except as animals act as passive carriers and disseminate the causative organisms (see chapters XXXV XXXVI and XXXVII)

OTHER ANIMAL DISEASES

There are several diseases distinctly animal in origin which have such a limited distribution or to which man has such slight susceptibility that they are not listed by the American Public Health Association

- Cowpox
- Foot and mouth disease
- Histoplasmosis
- Listerellosis
- Louping ill
- Milkers nodules

Milk sickness
Rift Valley fever
Sore mouth of sheep
Sporotrichosis
Swine erysipelas
Infections with animal parasites (other than amebic dysentery ascariasis and trichinosis)

The animal parasites which infect man as well as animals are mostly of small public health significance Two are listed by the American Public Health Association—amebic dysentery caused by the protozoan parasite *Amoeba histolytica* and trichinosis by the nematode *Trichinella spiralis* Ascariasis of animals is probably not transmitted to man

Other diseases caused by animal parasites many of which are not found in the United States are as follows

Protozoan Diseases

Balantidiasis (*Balantidium coli*)
Leishmaniasis cutaneous (oriental sore)
Leishmaniasis visceral (kala azar)
Trypanosomiasis African (sleeping sickness)
Trypanosomiasis American (Chagas disease)

Nematode Infections

Creeping eruption (*Ancylostoma braziliense*)
Guinea worm disease (*Dracunculus medinensis*)
Lungworm infection (*Metastrongylus elongatus*)
Sheep wireworm infection (*Haemonchus contortus*)
Strongyloidiasis (*Strongyloides stercoralis*)
Syngamus infection (*Sygamus laryngeus*)
Ternidens infection (*Ternidens diminutus*)
Trichostrongylosis (*Trychostrongylus* sp)

Cestode Infections

Broad fish tapeworm infection (*Diphyllobothrium latum*)
Dog tapeworm infection (*Dipylidium caninum*)
Dwarf tapeworm infection (*Hymenolepis nana*)
Echinococcus disease (*Echinococcus granulosus*)
Rat tapeworm infection (*Hymenolepis diminuta*)
Teniasis bovine (*Taenia saginata*)
Teniasis porcine (*Taenia solium*)

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- Foot and mouth disease
- Histoplasmosis
- Listerellosis
- Louping ill
- Milkers nodules

lesions of the lung and liver and the living animals spread enough organisms to be a menace to man Workers in slaughter houses are exposed to infection from hogs while the meat of infected hogs in some cases is capable of conveying infection if eaten without proper cooking (see chapter I)

Smallpox is a disease of man which cattle may contract but in a very modified form This was the belief of Jenner and has been substantiated by experimental evidence by several investigators When the infection has passed through the cow the virus will never again produce the symptoms of smallpox in man It will bring about a mild form of infection however which protects the individual against subsequent smallpox The administration of vaccine virus therefore has come to be the principal factor in the fight against smallpox It sometimes happens that a recently vaccinated individual will carry the infection of cowpox back to the cow thus starting an epidemic among cattle Susceptible persons may vaccinate themselves accidentally in caring for or milking such infected cattle (see chapter XI)

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Trematode Infections

Schistosomiasis (blood flukes *Schistosoma japonicum* and *Schistosoma mansoni*)
Lungfluke disease (lungfluke *Paragonimus westermani*)
Fascioliasis (liver fluke *Fasciola hepatica*)
Opisthorchiasis (liver flukes *Clonorchis sinensis* and *Opisthorchis felineus*)
Amphistomiasis (intestinal fluke *Amphistoma hominis*)
Echinostoma infection (intestinal fluke *Echinostoma ilocanum*)
Fasciolopsis infection (intestinal fluke *Fasciolopsis buski*)
Heterophyiasis (intestinal fluke *Heterophyes heterophyes*)

Virus dysentery in man is a respiratory infection with gastrointestinal manifestations (9) The causative agent may be the same as the virus causing scours (pneumoenteritis) of cattle (10) Further study is necessary on the problem

There are five diseases which are primarily human in origin but to which certain animals are susceptible They are of importance because infected animals may pass them back again to man They are as follows

Diphtheria	Smallpox
Septic sore throat	Tuberculosis (human type)
Scarlet fever	

Tuberculosis of human origin is rare in most animals The horse sheep goat cat and hen are difficult to infect artificially with this type of organism even when injected under the skin but spontaneous infection occurs in the dog and cow Guinea pigs are easily infected by injection but spontaneous infection with the human type of organism is rare and no known cases in man have been attributed to these animals Anthropoid apes and monkeys are even more susceptible than man to the human tubercle bacillus and close association with such infected animals might be dangerous to a person Parrots and cockatoos may contract the human type of tuberculosis and spread the organisms to persons associated with them through dust from the cage Hogs are as susceptible to the human as to the avian or bovine type but less often contract it spontaneously Butler and Marsh however found 30 per cent of the hogs fed on garbage from a tuberculosis sanitarium to be infected with the human type of organism Since the life of a hog is usually short such infection does not develop beyond the glandular stage Old hogs may show

The relationship of streptococci to udder infections of cows was suspected as early as 1884 by Nocard and Mollerau (4) In 1889 Bang produced inflammation of the udder of a cow by injecting into the milk duct a streptococcus isolated from a case of mastitis in another cow

Davis in 1915 distinguished *Streptococcus epidemicus* from the ordinary bovine streptococci This organism is included in the *Streptococcus pyogenes* group

THE ETIOLOGIC AGENT

Streptococcus pyogenes (25) is the term applied to a group of organisms found in various human infections Griffith (42) distinguished 23 types in the group They belong to Group A of Lancefield having in common various characteristics All of them form an erythrogenic toxin that usually causes a skin rash of greater or lesser degree They are relatively thermostabile *Streptococcus epidemicus* is the term usually applied to the member of the pyogenes group which causes septic sore throat

Bovine mastitis due to streptococci belonging to the Group B of Lancefield is quite common Formerly it was the practice to condemn milk in which any streptococci were found Now it has been shown that the ordinary mastitis streptococci are without public health significance

THE AFFECTION IN ANIMALS

The incidence of mastitis in cows is high and is of considerable economic significance In only a small proportion of the cases however is the trouble caused by a human pathogen David and Capps (10) applied a hemolytic streptococcus directly to an abrasion on the udder of a cow causing an infection as evidenced by the enormous number of streptococci found in milk but no external sign of inflammation caking or "gargety" milk In another experiment streptococci directly from a case of tonsillitis were introduced into the milk duct causing an infection of several weeks duration with numerous streptococci in the milk Their conclusions that streptococci of human origin may cause mastitis without external evidence of infection were soon corroborated by other investigators (21)

Smith and Brown (16) as well as Krumwiede and Valentine (12) showed that streptococci commonly associated with bovine mastitis could be differentiated from those causing human tonsillitis

CHAPTER XXXII

SEPTIC SORE THROAT

SEPTIC sore throat in man is caused by a member of the *Streptococcus pyogenes* group of organisms The organism is primarily a human pathogen but it may set up a focus of infection in the udder of the cow from whence it is transmitted back to man by way of the milk supply

HISTORY

Septic sore throat due to infected milk has been recognized in Great Britain for many years In 1875 there occurred at South Kensington England (1) several cases of sore throat and scarlet fever among 20 persons who had used cream coming from a district where there had been 119 cases of sore throat It is impossible to determine from the evidence presented whether this was a scarlet fever outbreak or a mixed infection of scarlet fever and septic sore throat

The first authentic record of an epidemic of the tonsillitis or quinsy type is that at Aberdeen (2) Among 110 families supplied by a single dairy 90 families were affected with 300 cases During the following years similar epidemics occurred with considerable regularity, the milk supply being incriminated by circumstantial evidence only

The first outbreak of septic sore throat recognized in the United States occurred in Boston Massachusetts in May 1911 Winslow (3) made a careful epidemiological study of the 1 400 cases involved finding that 70 per cent were supplied with milk from one dairy, the cases exactly coinciding with the two main delivery routes of that dairy The symptoms all pointed to a streptococcus as the infecting agent but there was little definite information available on this point In the laboratory of the Boston Board of Health as well as other laboratories no constant organism was found Theobald Smith however isolated streptococci from four cases at autopsy

that numerous reports of similar outbreaks appeared in the next few years In December 1911 and January 1912 an epidemic occurred in Chicago Illinois in which Capps and Miller (12) estimated 10 000 cases were involved traced to a milk supply supposed to have been pasteurized Mann (13) encountered an outbreak in Concord New Hampshire in January and February 1912 where 426 persons were made sick by the use of milk and cream from one dairy In February and March of the same year 602 cases with 28 deaths occurred in an epidemic in Baltimore Maryland where Frost (14) found 65 per cent of cases used one milk supply Veterinarians could find no mastitis in the cows of the suspected herd and it was thought that streptococci were introduced directly by infected persons In April and May 1913 North White and Avery (15) studied two epidemics involving 669 cases with 14 deaths which occurred simultaneously in different localities but having their source in the same dairy Two cows were found with acute udder inflammation from which streptococci were isolated that were identical with organisms isolated from the throats of several patients Smith and Brown (16) encountered 7 epidemics of septic sore throat which occurred in Massachusetts during 1913 and 1914 Krumwiede and Valentine (17) reported an outbreak of 232 cases in June 1914 at Rockville Center New York Armstrong and Parron (28) reported 42 outbreaks with 21 045 cases occurring between 1908 and 1926 all in northern United States In 1918 the United States Public Health Service began the compilation of milk borne epidemics of disease including septic sore throat (table 49)

In England (35) there were reported 21 epidemics with 2 039 cases during the period 1857 to 1929 In Denmark 3 098 cases occurred in epidemics during the same period In Canada (36) from 1906 to 1935 there were reported 3 epidemics involving 584 cases and 4 deaths

Practically all milk borne outbreaks of septic sore throat are traced to raw milk In a few instances milk has been improperly pasteurized or infected by a case or carrier after the pasteurization process was completed (table 49) *An instance is reported by Allen* and Baer (41) where powdered milk was contaminated by a case of septic sore throat in the kitchen in the process of reconstitution

The cow is responsible for two thirds of the cases of septic sore throat and four fifths of the deaths in milk borne epidemics (see table 50)

Frost and his associates (32) noted that not all animals harboring *Streptococcus epidemicus* may cause epidemics Only two cows out of 17 in which the organisms were found were associated with epidemics the other 15 cows apparently caused no human cases. The streptococci from all of them showed typical virulence when cultured Brooks (33) believes that while the types of streptococci which are common incidents of mastitis in dairy cattle apparently are not infective for man they may sometimes produce severe toxic disturbances especially in children when the organisms are present in milk in large numbers together with their toxins

The usual source of infection of the cow is an infected person Frost and Carr (26) recite their experience with an epidemic arising from a very high grade milk supply Laboratory examinations revealed enormous numbers of *Streptococcus epidemicus*—36 000,000 per cubic centimeter—in the milk of one animal A few days later a second cow was found infected and a little later still a third cow Cultures from the nose and throat of each person in the dairy revealed that two were carrying *Streptococcus epidemicus* One was a woman in the house who had no part in handling the milk the other was the hired man whose chief duties were the care of the cows and the milk After he left the dairy there was no more trouble

One quarter of the udder may be infected with streptococci without the other quarters becoming involved It is necessary therefore to examine milk from each quarter when looking for infection Cows once infected with *Streptococcus epidemicus* are likely to remain sources of danger over long periods of time and probably never should be returned to the milking line

Hadley and Frost found that cows could be quite easily infected by the simple process of smearing the teats with *Streptococcus epidemicus* and that mastitis subsequently developed The infected quarter usually lost its function of secretion because of the severity of the disease (34)

MILK BORNE OUTBREAKS

Although epidemics of septic sore throat of milk origin have been recognized in England for half a century and Swithinbank and Newman (11) in 1903 recorded that hardly a year passed without an outbreak yet it was not until 1911 that the disease was reported in the United States Winslow s (3) study of the Boston epidemic focused the attention of sanitarians on this cause of infection with the result

Table 49 Continued

Year	Place	Cases	Deaths	Milk Raw or Pasteurized
1935	Arkadelphia Ark	85	0	raw
1935	State Training School Red Wing Minn	114	0	raw
1935	Dansville N Y	13	0	raw
1935	Baldwinsville N Y	500	6	raw
1935	Patterson N Y	120	0	raw
1935	Corfu N Y	112	0	raw
1935	Wurtsboro N Y	26	0	raw
1935	Lewiston N C	16	1	raw
1935	Waynesboro Va	14	0	both
1936	Newington Conn	24	0	raw
1936	Greene County Ky	5	0	raw
1936	Belen N M	6	0	raw
1936	Fairlawn N J and 5 surrounding towns	17	7	raw
1936	Black Creek N Y	3	0	raw
1936	Dryden N Y	56	0	raw
1937	West Des Moines Ia	Note 1	0	raw
1937	Monterey Calif	250	0	raw
1937	Ponca City Calif	100	0	both
1938	Artesia and Los Alamitas Calif	4	3	raw
1938	Elizabeth Colo	5	0	raw
1938	Cobleskill N Y	33	0	raw
1938	Minetto N Y	63	0	raw
1938	Norwood N Y	75	4	raw
1938	Prospect N Y	20	0	raw
1938	Winnebago States Hospital Wisconsin	25	0	raw
1939	Fergus Falls Minn	274	0	raw
1939	Edmond Okla	200	?	raw
1939	Lawton Okla	100	0	raw
1939	Dublin N H	70	0	raw
1939	Catskill & Saugerties N Y	546	3	raw
1939	Medina N Y	92	0	raw
1940	Dighton and Taunton Mass	284	0	raw
1940	Waddington N Y	48	0	raw
1940	Worthington N Y	120	0	raw
1941	Huntington N Y	175	0	raw
1941	State Mental Hospital Wyo	11	0	pasteurized Note 2
1942	Alto Ga	111	0	pasteurized
1942	Pine Mt Ky	18	0	raw
1942	Cumberland and Benton Ky	47	0	raw
1942	Coxsackie N Y	00	0	raw
1943	Rowley Ma	Note 1	0	raw
1943	Albany County N Y	23	0	pasteurized
1943	Burnt Hills N Y			
1944	Forest Lake Minn	100	0	raw

Note 1 Septic sore throat and scarlet fever both reported
Note 2 Ice cream infected from discharging ear of ice cream maker

THE DISEASE IN MAN

In the study of the Boston epidemic of septic sore throat Winslow reported that the disease is a variable one and single cases may present hardly a feature in common with each other but any series of twenty cases shows at once its characteristic features

Table 49 —EPIDEMICS OF MILK BORNE SEPTIC SORE THROAT TABULATED BY OFFICE OF MILK INVESTIGATIONS

U S Public Health Service 1920-1944

YEAR	PLACE	CASES	DEATHS	MILK RAW OR PASTEURIZED
1920	Winchester Mass	43	0	raw
1922	Portland Ore	487	22	raw
1923	Arlington Mass	70	0	raw
1924	Danbury Conn	89	—	raw
1925	Nashua N H	42	0	raw
1925	Summit and Chatham N J	100	2	raw
1925	East Hampton Conn	45	0	raw
1925	Logan Ohio	332	1	raw
1925	Chester Pa	400	0	raw
1925	Mercer Pa	53	2	raw
1926	Pleasanton Calif	120	2	raw
1926	Guilford Conn	223	5	raw
1926	Hamden Conn	95	0	certified
1926	Brunswick Ga	900	0	certified
1926	Nashua N H	100	0	raw
1926	Madison Wis	80	0	raw
1928	Ramapo N Y	30	0	raw
1928	Lee Mass	950	48	raw
1928	Pottstown Pa	100	1	pasteurized
1929	Oskaloosa Iowa	100	3	raw
1929	Charlton Mass	84	2	raw
1929	Rochester Minn	200	0	raw
1929	Wayland N Y	141	1	raw
1929	Savannah N Y	75	1	raw
1929	Friendship N Y	14	0	raw
1929	Oxford Ohio	75	0	raw
1929	Baraboo Wis	250	6	raw
1930	Orange County Calif	20	0	raw
1930	Mt Desert Me	40	0	raw
1930	Ayer Mass	178	0	raw
1930	Wilbraham Mass	17	0	raw
1930	Schroon Lake N Y	11	0	raw
1930	Millbrook Village N Y	88	0	raw
1930	Kingston N Y	720	7	raw
1930	Clyde N Y	12	0	raw
1930	McMinnville Ore	30	0	raw
1931	Kentland Ind	200	0	raw
1931	Lancaster Ohio	103	0	improperly pasteurized
1931	Oxford Ohio	127	0	raw
1931	Walton N Y	444	7	raw
1931	Greenwich N Y	32	0	raw
1931	Oyster Bay N Y	117	1	raw
1931	Marion Mass	17	0	raw
1932	Topsfield Mass	20	3	raw
1932	Milton Wis	30	0	raw
1932	Belton Tex	100	0	raw
1933	Chilton Wis	250	2	raw
1933	Mt Solon Va	11	0	raw
1933	Carbondale Pa	3	1	raw
1933	W Luzerne and T Hadley N Y	179	2	raw
1933	Rockville Conn	34	0	raw
1934	Flemington N J	131	2	raw
1934	Potsdam N Y	91	4	raw
1934	Waterloo N Y	55	0	raw
1934	Lewisburg W Va	38	0	raw
1934	University of New Hampshire	32	0	raw

epidemics indicated that there was no difference to susceptibility by sex and that the age distribution of cases corresponded closely to the age distribution of the population of the community in which the epidemics occurred The amount of milk consumed had a direct bearing upon the probability of infection the attack rate varying directly with the quantity of milk (containing the infectious material) which a person drank irrespective of age

PREVENTION

The prevention of milk borne outbreaks of septic sore throat depends upon two factors

1 Rigid precaution in the prevention of udder infection of cattle by human cases of sore throat

2 Proper pasteurization of all milk supplies

Since udder infection with *Streptococcus epidemicus* often produces no apparent evidence of its presence cases of mammitis often go unrecognized till a considerable amount of damage has been done Even in certified dairies with regular examination of both employees and cattle Frost Gumm and Thomas found by laboratory examination four cows infected with *Streptococcus epidemicus* Ordinary market milk therefore especially requires careful pasteurization as a supplementary protection

Brooks (37) has emphasized the necessity in an extensive outbreak of septic sore throat lasting several days of looking for the cow which is causing the trouble A person who is a carrier of *Streptococcus epidemicus* may contaminate the milk once but not usually several days in succession After the cow which is harboring virulent streptococci has been found then it is necessary to find the person who is harboring the germs in his throat that infected the cow

Pasteurization as a means of destroying milk streptococci has been much studied by numerous investigators It would appear that the bovine species are so heat resistant that some of them will withstand 143 F for sixty to ninety minutes and can subsequently be demonstrated in small numbers in the milk The human types on the other hand are quite susceptible to pasteurizing temperatures and are entirely destroyed within the allotted time

Park (27) collected 100 strains of streptococci from cases of septic sore throat tonsillitis scarlet fever mastoiditis glandular fever erysipelas and other human sources finding every one of them killed

Table 50—Sources of Infection in 61 Milk Borne Outbreaks of Septic Sore Throat with Cases and Deaths for Each Source
U S 1928-1944
(Compiled from statistics of U S Public Health Service)

Source of Infection	Number of Outbreaks	Total Cases	Total Deaths
Case	20	2240	22
Carrier	13	574	0
Infected finger	4	245	0
Cow	24	5098	83
	61	8157	105

The incubation period is short about two days The onset of at tack is rapid often accompanied by severe headache and acute grippy pains The temperature is high reaching 103°F to 105 F The throat is variable At first there is a diffuse redness extending over the tonsils simulating scarlet fever Later, small isolated patches of white appear resembling ordinary follicular tonsillitis Still later many cases may show an extensive membrane like exudate similar to that in diphtheria

The first stage of the disease lasts 3 to 5 days in which there is great prostration *The patient entirely recovers in a short time pro* vided there are no complications Numerous cases however show such complications as abscesses in the peritonsillar region and cervi cal glands Very severe cases may result in rheumatism pneumonia nephritis or pericarditis Death never follows the original infection but may be the result of a complication

In the 1928 epidemic at Lee Massachusetts the cases were dis tributed among the different age groups as shown in table 51

A further study of that epidemic indicated that 45 per cent of sick families had 1 case 28 per cent had 2 cases and 27 per cent had 3 cases

Table 51—Epidemic of Septic Sore Throat at Lee Mass Showing Age Groups Affected

Age	1 000 Cases	40 Deaths
0-15	20 per cent	3 per cent
16-29	28 per cent	3 per cent
30-44	22 per cent	3 per cent
45-59	19 per cent	31 per cent
60 and over	11 per cent	60 per cent

The experience in the Lee epidemic that children were somewhat less prone to infection than other age groups has been confirmed in England (38) Studies in New York State (39) covering a series of

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after an exposure of 10 minutes at 140°F or 30 minutes at 138°F The destruction of many of the organisms was surprisingly rapid some showing no growth after 5 minutes at 138°F

ITEMS OF NOTE

1 Septic sore throat is primarily a human infection
2 The causative agent may find lodgement in the milk ducts of the cow without necessarily producing any pathologic lesion
3 The ordinary streptococci of bovine origin do not cause sore throat in man
4 Enormous numbers of streptococci may be eliminated from the infected udder of a cow, causing an acute outbreak of sore throat among persons drinking the milk
5 Proper pasteurization of all milk supplies is the only sure safe guard against such epidemics

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In 1923 Dick as well as Dochez differentiated the scarlet fever streptococcus from other organisms in the group making bacteriologic evidence possible Jones (9) and others isolated typical scarlet fever streptococci of human origin from the udder of a cow

THE ETIOLOGIC AGENT

Streptococcus scarlatinae (25) is the term usually applied to the member of the *Streptococcus pyogenes* group which causes scarlet fever It is a hemolytic organism belonging to serologic Group A It produces a specific exotoxin which can be neutralized by antitoxin (See also Septic Sore Throat chapter XXXII)

THE INFECTION IN ANIMALS

Jones and Little (9) were the first to furnish bacteriologic evidence that cows could be infected with scarlet fever streptococci In a scarlet fever outbreak of 200 cases studied by the New Jersey State Department of Health the usual relation of a case of scarlet fever on one of the farms supplying the milk was found More careful observations indicated that one of the cows was suffering from an acute injury of the teat An investigation by Jones and Little of the milk from this cow indicated that as many as 345 000 000 streptococci per cubic centimeter were being eliminated The organisms answered all the necessary requirements of scarlet fever streptococci of human origin (10)

Injection of these organisms into one of the other teats of the same cow produced no abnormality nor could streptococci be found in the milk from that quarter until still another quarter was injected when both of these showed streptococci which gradually diminished in two weeks

A normal cow was injected by means of a teat tube with 15 to 20 of the scarlet fever streptococci isolated from the first cow There was a severe general reaction beginning within two days with severe fever and reddening of the skin The udder was swollen and the milk purulent On the second day 1 200 000 000 streptococci per cubic centimeter were eliminated The injection of another teat of this cow resulted in a condition similar to the second injection of the other cow in that the quarter showed no abnormalities but excreted for a time a comparatively small number of organisms (556 000 per c c at the most) This would indicate a lack of immunity of the other quarters when infection existed in one quarter

CHAPTER XXXIII

SCARLET FEVER

SCARLET FEVER is primarily an infectious disease of man caused by a member of the *Streptococcus pyogenes* group of organisms. Cows may become infected from human sources and pass the disease back to man through the milk.

HISTORY

The responsibility of the cow for scarlet fever epidemics was suggested from time to time in the absence of other evidence. Power (1) in 1882 attributed an outbreak to contamination by a cow suffering with puerperal fever. Klein at the same time showed that cows inoculated subcutaneously with material from a human case of scarlet fever developed an abscess at the site of inoculation and material from such an abscess could produce a similar lesion when injected into another cow.

In 1885 Power (2), Cameron (3) and Klein (4) encountered another epidemic which they attributed to bovine origin, lacking any human sources. A vesicular eruption on the udder and buttocks of several animals accompanied by constitutional symptoms and discharge from the eyes and nose with sore throat (Hendon disease) was thought to be the cause. Russell (5) in 1888, Hill (6) in 1890 and Jones (7) in 1909 all reported similar instances where a milk epidemic of scarlet fever occurred and cows in the responsible herd were found suffering from a condition similar to that described by Power, Klein and Cameron. Bacteriologic evidence was of course entirely lacking.

Busey and Kober (8) in 74 epidemics included in Trask's compilation state that in 20 instances the infection was attributed to disease among the milk cows. In 4 cases the puerperal condition of the cow is blamed, in 9 there was disease of the udder or teats, in 6 there was loss of hair and casting of the skin, while one cow was suffering from a febrile condition.

Table 52 —MILK BORNE EPIDEMICS OF SCARLET FEVER TABULATED FROM REPORTS OF U S PUBLIC HEALTH SERVICE 1919-1944

YEAR	PLACE	CASES	DEATHS	MILK RAW OR PASTEURIZED
1919	Greenwich Conn	18	0	raw
1919	Orange N J	10	0	raw
1920	Providence R I	31	0	pasteurized
1921	Ossining N Y	24	0	—
1922	Croton N Y	44	1	—
1922	Huntington N Y	?	?	—
1922	Jamestown N Y	25	—	—
1922	Beloit Wis	17	1	raw
1923	Winchestertown Mass	7	0	raw
1923	Kewanee Ill	23	1	raw
1923	Madison Wi	33	0	raw
1923	Buffalo N Y	57	3	pasteurized
1923	Pittsfield Mass	8	0	raw
1923	San Bernardino Calif	208	2	raw
1924	Helena Mont	38	0	raw
1924	Pittsfield Mass	7	0	raw
1924	Bristol Conn	133	0	raw
1924	Cohoes N Y	82	—	raw
1924	Pontiac Mich	5	0	raw
1925	Helena Mont	11	1	raw
1925	Binghamton N Y	25	0	raw
1925	Binghamton N Y	19	0	raw
1925	Scio Ohio	81	2	raw
1926	Clinton Mass	80	0	raw
1926	St John Mich	59	0	raw
1926	Lakefield Minn	67	0	raw
1926	Deposit N Y	51	2	raw
1926	Troy N Y	14	1	raw
1927	Washington N J	199	0	raw
1927	Riverside & Paramus N J	9	—	raw
1927	Schuylerville N Y	9	0	raw
1927	Kalispell Mont	139	3	raw
1927	Janesville Wis	22	2	raw
1928	Farmington Conn	52	0	raw
1928	Avon Conn	108	4	raw
1928	Lansing Mich	93	1	raw
1928	Guilford N Y	31	0	raw
1928	LaCrosse Wis	20	1	raw
1928	Grant Park Ill	37		raw
1928	Edwardsville Ill	13		raw
1928	Pembroke and Marshfield Mass	15	0	raw
1929	Alexis Ill	36	0	raw
1929	Ottawa Ill	86	1	raw
1929	Berea Ky	350	0	both
1929	Framingham Mass	15	0	raw
1929	Plymouth Mass	150	0	raw
1929	Berlin N H	278	0	
1929	New Hartford and Utica N Y	6	0	raw
1929	Skaneateles N Y	6	0	raw
1929	Jackson Tenn	74	0	raw
1929	Spokane Wash	31	0	raw
1929	LaCrosse Wis	20	0	raw
1930	Grand Island Neb	32	0	raw
1930	Farrell Pa	10	0	raw
1931	Alton Ill	9	0	raw
1931	Mansfield Willimantic Conn	100	2	raw
1932	Decatur Ill	13	1	raw
1932	Brockton Mass	8	0	pasteurized

Animals other than the cow are probably of small importance in the spread of scarlet fever Reports have been made from time to time concerning infection of dogs in contact with human cases but all lack bacteriologic confirmation Numerous attempts were made before the discovery of *Streptococcus scarlatinae* to induce infection in laboratory animals with material direct from human cases but all were unsuccessful Several workers were able to produce lesions in monkeys and chimpanzees with human material while others failed The failure of Hektoen and Weaver in producing the disease in monkeys fed on milk to which had been added material from the throats of scarlet fever patients, is explained by the work of Jones (9)

Since 1923 experimental infection has indicated the susceptibility of certain animals The dog is highly susceptible to the infection of a living culture of the organism succumbing in 3 to 5 days from an acute hemorrhagic nephritis Killed cultures and culture lysates are also highly toxic for dogs (12) Goats are quite susceptible to scarlet fever toxin and have been used to a certain extent as a substitute for human subjects in standardizing such toxin Mice rats guinea pigs cats chickens pigeons monkeys calves and sheep have been found entirely unsusceptible to toxin while rabbits and pigs give conflicting results (13)

MILK BORNE EPIDEMICS

Many outbreaks of scarlet fever have been attributed to contaminated milk supplies in the past Trask (8) listed 125 such epidemics which occurred prior to 1908 Armstrong and Parron (14) added 40 more outbreaks in the United States from 1908 to 1926 All occurred in the northern states southwestern Ohio being the most southern locality In Canada Murray (15) tabulated 7 epidemics embracing 192 cases that occurred between 1906 and 1935 there were no deaths In England Wahby (16) reported 88 epidemics with 7 650 cases from 1857 to 1929

In table 52 are listed 108 epidemics which have been recorded in the United States during the period 1919 1944

Jones (11) claims that usually milk borne epidemics of scarlet fever are not due to a human case or carrier on the farm or in the dairy Milk is not only an inhibitive agent in which such organisms fail to grow, but it contains an active principle which greatly diminishes the number of streptococci at room temperature He concludes that "the opinion that severe outbreaks of scarlet fever result

from human contamination of milk must be viewed with considerable doubt" It is possible that a few individuals may contract the disease through direct human contamination of the milk but the occurrence of epidemics would imply a much heavier inoculation of the milk than would be probable by this means The enormous numbers of streptococci shed from the udder of a single cow infected with this organism may contaminate a large bulk of milk and even after some of the streptococci have perished still show sufficient numbers of living organisms to infect man This is a reasonable explanation of milk borne epidemics

The figures from the United States Public Health Service (table 53) would indicate that the cow was implicated in only one fourth

Table 53—Sources of Infection in 65 Milk borne Outbreaks of Scarlet Fever with Cases and Deaths for Each Source United States 1928-1944
Compiled from Statistics of the U S Public Health Service

Source of Infection	Number of Outbreaks	Total Case	Total Death
Case	38	1437	11
Carrier	9	836	9
Infected finger	2	13	0
Cow	16	1924	19

of the milk borne outbreaks Complete bacteriologic examinations were not carried out in all outbreaks however The outbreaks which were traced to the cow were responsible for more than a third of the cases and half of the deaths

PREVENTION AND CONTROL

The prevention of scarlet fever of animal origin requires attention to several details First no human case of scarlet fever must have contact with lactating cows Even a few organisms will be sufficient to infect the teats In the presence of a suspected milk borne epidemic of scarlet fever careful examination must be made of all cows in the herd for possible infection Finally pasteurization of the milk will be a complete safeguard for scarlet fever streptococci are easily killed by heat at 140 F for 30 minutes

ITEMS OF NOTE

1 Scarlet fever is primarily a human infection
2 Cows may become infected in the udder shedding enormous numbers of scarlet fever streptococci into the milk

Table 52 Continued

YEAR	PLACE	CASES	DEATHS	MILK RAW OR PASTEURIZED
1932	Bridgewater New Berlin N Y	29	0	raw
1932	Elizabeth N J	14	0	raw
1932	Sweetwater Tex	42	0	raw
1933	Thomaston and Plymouth Conn	100	1	raw
1933	Hingham Weymouth and Quincy Mass	43	2	raw
1933	East and West Bridgewater Mass	95	1	raw
1934	Anaheim Calif	14	1	raw
1934	Hampton Iowa	25	0	raw
1934	*Fenton Sanford and McDonough N Y*	92	1	?
1935	Westbury, N Y	5	0	raw
1936	Moline Ill	182	0	raw
1936	Kewanee Ill	27	0	raw
1936	Belen N M	14	0	raw
1936	Wellesville N Y	196	6	raw
1936	Emeryville N Y	16	0	raw
1936	Red Creek N Y	73	2	raw
1936	*Wayne & Tyrone* N Y	16	0	raw
1936	Pottersville N Y	8	0	raw
1936	Owego N Y	511	6	raw
1936	Bradford Pa	55	0	raw
1936	Combined Locks Kimberly and Little Chute Wis	108	1	raw
1936	Menasha Appleton and Neenah Wis	76	1	raw
1937	Rockford Ill	93	1	raw
1937	Emmett Township Mich	25	1	raw
1937	Suttons Bay, Mich	67	0	raw
1937	*Hannibal Mo*	17	0	raw
1937	Bethlehem Township N Y	17	0	raw
1937	Chatanqua Township N Y	17	0	raw
1937	Starkey Township N Y	9	0	raw
1937	Woodward Okla	45	1	both
1937	Ponca City Okla	25	0	both
1937	Carrizo Springs Tex	9	0	raw
1937	Burlington Vt	65	0	raw
1937	West Des Moines Ia	Note 1	—	raw
1938	Gardner Ill	36	0	raw
1938	Jordanville and Richfield Springs N Y	14	0	raw
1938	Guthrie Okla.	2	0	raw
1938	Hancock Wis	4	0	raw
1938	Newberg Wis	26	0	raw
1939	Hornell City N Y	18	0	raw
1939	Canton Ohio	21	1	raw
1939	Lawton Okla	3	0	raw
1940	Casey, Ill	24	0	raw
1940	Binghampton N Y	6	0	raw
1941	Pulteney N Y	33	0	raw
1942	Greenview Ill	39	0	raw
1942	Cannonsville N Y	44	0	raw
1943	Rowley Mass.	Note 1	0	raw
1944	Richland Center Wis	71	0	raw

Note 1 Scarlet fever and septic sore throat both reported

CHAPTER XXXIV

DIPHTHERIA

DIPHTHERIA is primarily an infectious disease of man caused by *Corynebacterium diphtheriae* On rare occasions animals may become infected thus acting as a source of infection for man

THE ETIOLOGIC AGENT

The diphtheria bacillus *Corynebacterium diphtheriae* does not invade the tissues but localizes on a mucous member such as the throat of man or in wounds where it produces a powerful toxin

There are several other members of the genus *Corynebacterium* which are found in animals but which have little significance for man Merchant (20) mentions four types associated with diseases of domestic animals

C pyogenes is a pus producing organism which infects cattle sheep and swine

C pseudotuberculosis is found in horses cattle and sheep

C renalis infects cattle principally but has been found in sheep and horses Olafson in one instance encountered it in a dog It pro duces no toxin

C equi is found in pulmonary infections of horses in lymph gland infections of swine and in normal cows milk

Brooks and Hucker (21) studied a large number of cultures of diphtheroids from animal sources finding that morphologically they showed a marked degree of variation

ANIMALS SUSCEPTIBLE

There have been reported in the past a considerable number of instances of infection of dogs cats and fowls with *C diphtheriae* Bacteriologic evidence however is either entirely lacking or is faulty with diphtheroid organisms often mistaken for true diph theria bacilli

3 Milk, under ordinary conditions prevents the growth of scarlet fever streptococci even killing them to a certain extent
4 Prevention of milk borne scarlet fever requires first that cows be kept free from contact with human cases of scarlet fever and second proper pasteurization of all milk
5 Animals other than the cow are probably of little importance in the spread of scarlet fever

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CHAPTER XXXIV

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Cats have been found by several investigators to be susceptible to diphtheria toxin as well as to the bacilli When injected subcutaneously either with toxin or with live cultures such animals exhibit definite symptoms and often die Klein (1 2) Brodie (3), Yabe (4) Klein (5) rubbed cultures into the cornea of cats as well as injected intratracheally with definite results Infection by feeding the organisms in milk was unsuccessful however Intratracheal inoculations were successfully made by Welch and Abbott (6) with the production of membranes from which the organisms could be recovered Henke was unsuccessful in the production of membranes

Savage (7) sought to determine experimentally whether cats were capable of harboring diphtheria bacilli The implantation of large numbers of virulent organisms into the nasal cavities were ineffective in setting up any general or local lesion The same was true when massive doses were applied to the throat by swabs The organisms survived but a short period of time usually disappearing within twenty four hours Savage believes that the mucous membranes of cats are unfavorable for the growth or persistence of the diphtheria bacillus and that cats do not serve as carriers of diphtheritic infection *He analyzes the epidemiologic evidence of previous* cases reported concluding that the view that cats can acquire the disease naturally is entirely without foundation

Simmons (8) on the other hand found two cats harboring true diphtheria bacilli one in the nasal fossa and the other in lesions of the vocal cords The first animal developed a croupy cough was unable to swallow, and cried continually About a week after the cat developed this condition a woman with whom the cat slept developed a typical case of diphtheria which proved fatal The organisms isolated from both the woman and the cat were virulent for guinea pigs as proved by the injection of two animals one of which was protected by antitoxin

Domestic fowls were found by Litterer (9) capable of not only harboring diphtheria bacilli but of transmitting the disease to man Two hundred and fifty six human cases suffering from acute or carrier diphtheritic infection were investigated where the family owned fowls suffering from roup fowl diphtheria cholera etc A total of 1 126 sick fowls were examined in two flocks several fowls were found harboring virulent diphtheria bacilli as proved by morphologic and virulence tests In each instance a child in the family owning the fowls showed similar virulent organisms Successful

inoculations of the virulent diphtheria organisms isolated from both the fowls and the children were made into other fowls suffering from roup later the infection in the experimental fowls was cured with diphtheria antitoxin

Horses are quite susceptible to diphtheria toxin when injected for the purpose of producing antitoxin and consequently consider able care must be used on initial injections True diphtheria occurs but rarely however Cobbett (16) reports such a case in a pony infected by its rider Minett (17) likewise recorded several cases of ulcerative lymphangitis in horses infected with diphtheria bacilli probably from human cases

Other animals exhibit some susceptibility to toxin but apparently do not contract the disease naturally Sheep have been used to some extent for the production of antitoxin and may succumb from over doses of toxin as noted by Roux and Yersin in 1889 Wernicke in 1893 likewise killed a sheep by gradually increasing the doses of diphtheria culture Goats have been used for the production of diph theria antitoxin for toxin antitoxin mixtures Ledingham found that goats would succumb to large injections of toxin (250 c c) Wladim iroff injected diphtheria cultures into the teats of three lactating goats Only one of them exhibited any constitutional symptoms Diphtheria bacilli were found in the milk for a period of six days but they rapidly diminished in numbers Dogs have been utilized by various workers in experimental investigations They are susceptible to injection of both toxins and cultures Unconfirmed reports of natural diphtheria infection in dogs have been recorded Brandt in 1908 obtained from a dog a culture which he considered true diph theria but it did not kill guinea pigs when injected Hull had cases reported of diphtheria infection in dogs but complete laboratory confirmation was lacking

The laboratory animals vary in susceptibility Rats and mice are quite immune Guinea pigs are very constant in susceptibility and hence are the animals of choice in experimental work The standard ization of both diphtheria toxin and diphtheria antitoxin is based upon the amount of toxin required to kill a guinea pig weighing 250 grams in four days

Monkeys were found by Burnet in 1910 rather resistant in infec tion Seventeen experiments were made by rubbing virulent cultures into the abraded mucous membrane of young animals Eleven experi ments were entirely negative in five the results were slight while

in one animal which was ill at the time of inoculation, the lesions were extensive

Eels were shown susceptible to diphtheria toxin by Pettit on two occasions while alligators were found highly susceptible by Metchnikoff Frogs, when injected with toxin remained well at low temperatures but developed paralysis when maintained at 37°C

INFECTION IN COWS

Cows are quite susceptible to diphtheria toxin They have been recommended from time to time as a substitute for the horse in the production of antitoxin, but they are not altogether satisfactory *Diphtheria bacilli when injected under the skin were found by* Klein (2) to kill cows in as short a period as eleven days Fifteen animals so treated either died or showed marked reactions Wladimiroff had a similar experience but Abbott (10) could not confirm Klein s findings on two cows with which he worked

Cows fed diphtheria bacilli by mouth exhibited no ill effects (Klein) Diphtheria bacilli injected into the udder through the teat by Wladimiroff killed a cow in ten days although diphtheria toxin administered in the same way caused no trouble

Dean and Todd in 1902 (11) found two cows with scabby teats *from which diphtheria bacilli were isolated The animals were im*plicated in a diphtheria epidemic The authors concluded that the cows were infected by the milker Ashby in 1906 (12) similarly found diphtheria bacilli in ulcers on the teats of a cow implicated in an epidemic The milker of the cow however was probably responsible for this condition since he lived in the house where the first case of the epidemic originated

Henry (13) describes an epidemic of 32 cases where a cow was involved A girl who did the milking had a lesion on the finger which proved to be harboring diphtheria bacilli With her removal the *epidemic ceased only to flare up again two weeks later It was* found that one of the cows had developed a sore on its teat which harbored diphtheria bacilli The organisms isolated were virulent by the usual protection tests

Graham and Golaz (14) reported a cow with sores on the teats covered with thick black scabs When the scabs were removed a ragged ulcerated surface was left that exuded a mucopurulent fluid The teats were *tender and the sores did not heal Cultures* showed virulent diphtheria bacilli present An investigation revealed

that the cow had been infected by a milker who was a diphtheria carrier This cow was responsible for fifty two cases of diphtheria mostly among adults

Since diphtheria bacilli localize at the point of entry and produce a toxemia rather than a bacteremia such organisms do not find their way into the milk of infected cows unless the primary lesions are on the teats or udder Instances of cutaneous diphtheria on the teats or udder of the cow as cited above may be even more numerous than reported *Cases of true mastitis or udder infection with the* diphtheria bacillus have not been reported and it is not known whether they occur under natural conditions or not

MILK BORNE EPIDEMICS

Numerous epidemics of diphtheria spread by cow s milk have been reported In 1908 Trask (15) collected 51 such records which had occurred up to that time and Armstrong and Parron (18) added 25 more from 1908 to 1926 in the United States In the latter study pasteurized milk was implicated once certified milk once ice cream once and butter once The epidemics were mostly in the northern states although one epidemic occurred at Austin Texas and one at Charlottesville Virginia In England from 1857 to 1929 there were 42 such epidemics recorded with 3 433 cases

Milk in such instances has been commonly thought to receive its contamination with virulent diphtheria bacilli directly from a human carrier or case either on the farm where the milk is produced or en route to consumer

Recently the number of milk borne epidemics of diphtheria has fallen off From 1918 to 1944 only eleven are on record (table 54)

Table 54 —MILK BORNE EPIDEMICS OF DIPHTHERIA IN THE UNITED STATES

		CASES	DEATHS	MILK
1918	Old Town Me	10	0	raw
1928	Bricks N C	38	0	raw
1931	Crandon Wis	22	0	raw
1933	Idaho Falls Idaho	7	2	raw
1933	Santa Barbara Co Calif	12	1	raw
1934	Lincoln Kan	9	0	raw
1938	Pueblo Colo	31	3	raw
1941	Webster City Iowa	5	0	raw
1943	Hood River Ore	20	4	raw

This is partly due to increased pasteurization of milk and partly due to the decreased incidence of diphtheria in the population

in one animal which was ill at the time of inoculation the lesions were extensive

Eels were shown susceptible to diphtheria toxin by Pettit on two occasions while alligators were found highly susceptible by Metchnikoff Frogs when injected with toxin remained well at low temperatures but developed paralysis when maintained at 37°C

INFECTION IN COWS

Cows are quite susceptible to diphtheria toxin They have been recommended from time to time as a substitute for the horse in the production of antitoxin, but they are not altogether satisfactory Diphtheria bacilli when injected under the skin were found by Klein (2) to kill cows in as short a period as eleven days Fifteen animals so treated either died or showed marked reactions Wladimiroff had a similar experience but Abbott (10) could not confirm Klein s findings on two cows with which he worked

Cows fed diphtheria bacilli by mouth exhibited no ill effects (Klein) Diphtheria bacilli injected into the udder through the teat by Wladimiroff killed a cow in ten days although diphtheria toxin administered in the same way caused no trouble

Dean and Todd in 1902 (11) found two cows with scabby teats from which diphtheria bacilli were isolated The animals were implicated in a diphtheria epidemic The authors concluded that the cows were infected by the milker Ashby in 1906 (12) similarly found diphtheria bacilli in ulcers on the teats of a cow implicated in an epidemic The milker of the cow however was probably responsible for this condition since he lived in the house where the first case of the epidemic originated

Henry (13) describes an epidemic of 32 cases where a cow was involved A girl who did the milking had a lesion on the finger which proved to be harboring diphtheria bacilli With her removal the epidemic ceased, only to flare up again two weeks later It was found that one of the cows had developed a sore on its teat which harbored diphtheria bacilli The organisms isolated were virulent by the usual protection tests

Graham and Golaz (14) reported a cow with sores on the teats covered with thick black scabs When the scabs were removed a ragged ulcerated surface was left that exuded a mucopurulent fluid The teats were tender and the sores did not heal Cultures showed virulent diphtheria bacilli present An investigation revealed

SECTION FOUR

ANIMALS AS PASSIVE CARRIERS OF DISEASE ORGANISMS

The cow was not implicated in all of the epidemics due to milk In some instances contamination of the milk occurred after it left the cow from a human case of diphtheria, or from a carrier

ITEMS OF NOTE

1 Diphtheria is primarily an infection of man
2 On rare occasions animals may become naturally infected from human sources
3 Most of the reports in the literature of animal infection are unconfirmed by complete laboratory diagnosis
4 The cat is a doubtful menace chickens have been found harboring virulent diphtheria bacilli horses may contract the infection
5 The cow may become infected upon the udder and thus be a serious menace by way of the milk supply

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CHAPTER XXXV

BOTULISM

BOTULISM is an acute toxemia caused by the toxin of one of the botulinum group of bacteria The toxin is usually ingested in foods in which this organism has grown

HISTORY

The first case of botulism to be recorded according to Dickson (2) occurred in 1735 The disease was given its name by Mullen in 1870 because meat products were supposed to be responsible hence botulism from the Latin botulus sausage Numerous cases and out breaks occurred in the years that followed but little was added to the knowledge of the disease In 1895 van Ermengem (6) studied an outbreak involving thirty four cases and three deaths The causative agent was isolated from a ham which the patients had eaten and was named *Bacillus botulinus*

Meyer has listed 367 human outbreaks of botulism which oc curred in the United States from 1899 to 1942

Buckly and Shippen (11) called attention to the disease in ani mals in 1917

THE BOTULINUM ORGANISMS

There are a number of different organisms closely related which cause botulism Bengston (1) divided them into five types

Type A Cause of most American outbreaks from canned foods
Type B Cause of a few American outbreaks
Type C No human outbreaks Cause of outbreaks in wild aquatic birds
Type D No human outbreaks Low toxicity for man
Type E Cause of a few human outbreaks

Bergey classifies *the organisms into two groups Clostridium botulinum* includes types C D and E They are non proteolytic

food The organisms were also found in tannery waste sludge by Greer (10)

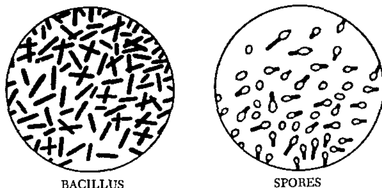


Fig 74 —*Clostridium botulinum*

THE DISEASE IN ANIMALS

Horses develop botulism from eating moldy or spoiled hay corn or other feed in which botulinum toxin has been produced The dis ease is manifested by loss of muscular control sometimes called 'blindstaggers Bacteriologic confirmation is often lacking how ever and no accurate figures are available on the extent of the dis ease

Cattle are rather infrequently infected although outbreaks have been reported by Graham and Schwarze and others Spoiled hay and other feed in which the toxin has developed is usually the cause The disease has been described in cattle in France by Rossi and Vigel with symptoms in the bovine similar to those occurring in man

Hogs sheep and dogs show a marked resistance to botulism and do not develop the disease from natural causes Goats however are susceptible Among the laboratory animals cats rabbits guinea pigs and mice are extremely susceptible to subcutaneous injections of the toxins white rats frogs and fishes are almost completely re sistant

Botulism afflicts various birds One cause of limber neck in chick ens is toxin of *Cl botulinum* type C Remnants of foods which have caused illness and death among human beings have frequently caused limber neck and death when thrown to chickens Such out breaks among fowls are not uncommon Two outbreaks occurred in

Meyer and Gunnison found fifteen sub types in this group on the basis of toxicity agglutination and fermentation *Clostridium para botulism* includes types A and B They are proteolytic and grow more easily than the other types They are apparently more common in the United States and hence are the cause of more outbreaks of food poisoning

The toxin formed by the organisms under suitable conditions of anaerobiosis and non acidity is one of the most powerful poisons known (table 55) It is an exotoxin absorbed through the intestinal

Table 55 —BOTULINUM TOXIN COMPARED WITH OTHER POWERFUL POISONS (13)

	MINIMAL LETHAL DOSE PER KILOGRAM OF BODY WEIGHT
Botulinum toxin (dried)	0 00012 milligrams
Tetanus toxin (precipitated)	0 0033
Cobra venom (dried)	0 002
Ricin	0 03
Strychnine	0 06
Potassium cyanide	1 9
Diphtheria toxin (filtrate)	2 0 cubic millimeters

tract It is neurotoxic either by feeding or by injection The toxin formed by each organism is neutralized by its homologous antitoxin

The spores are very resistant to heat One strain was reported by Easton and Meyer (3) to withstand 212°F for 330 minutes (table 56) Such heat resistance is of significance in food preservation by canning

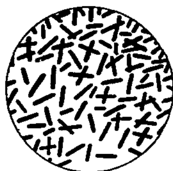
Table 56 —HEAT RESISTANCE OF BOTULINUM SPORES

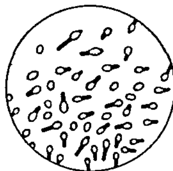
Botulinum spores require the following period of time at different temperatures for destruction

4 minutes	at 120 C	(248 F)
10	at 115 C	(239 F)
32	at 110 C	(230 F)
100	at 105 C	(221 F)
330	at 100 C	(212 F)

The spores are widely distributed in nature Since the organisms are strict anaerobes, they probably grow symbiotically in soil with aerobes In view of the wide distribution in nature the organisms would be expected to be present occasionally in intestinal tracts of man and animals Dickson and Burke isolated them from the feces of a hog and Easton and Meyer from the feces of three hogs and two cattle Tanner and Dack isolated them from two of ten specimens of feces from normal individuals This does not necessarily mean that man is a carrier of the spores but that the organisms may enter and pass through the intestinal tract should they happen to be on green

food The organisms were also found in tannery waste sludge by Greer (10)





BACILLUS SPORES

Fig 74—*Clostridium botulinum*

THE DISEASE IN ANIMALS

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1910 with 103 outbreaks during the next ten years Fifty six of these occurred in California and 31 in the State of Washington with the others in Colorado 2, District of Columbia 1, Illinois 1 Indiana 1 Michigan 1 New Jersey 1, Nevada 5 and Oregon 4 In 22 instances the outbreaks in chickens were caused by careless disposition of food which had caused human outbreaks and to which the chickens had access

Botulism in wild ducks has been described by Quortrup and Holt (12) *In shallow waters which serve as feeding grounds for these birds* the vegetation produces an oxygen deficient condition which is ideal for the production of botulinum toxin *Cl botulinum* type C is the causative agent

HOMECANNED OR HOMEPREPARED FOOD
RESPONSIBLE FOR OUTBREAKS OF
BOTULISM

Fig 75 —Cases of botulism in man from various sources (after Meyer)

THE DISEASE IN MAN

The symptoms of botulinum intoxication compared with other food poisonings are given in table 18

In the United States the mortality from botulism has been about 65 per cent while in Europe it has been much lower around 25 per cent Reasons for this are obscure Possibly European strains are less toxic

Meyer collected figures on 367 outbreaks of botulism involving 1 052 cases and 678 deaths which occurred in the United States from 1899 to 1942 (*table 57*) Commercially canned products were responsible for 83 outbreaks Factory canners and packers studied

Table 57 —BOTULISM IN THE UNITED STATES AND CANADA 1899-1942

367 outbreaks 1 052 cases with 687 deaths or 65 per cent case fatality rate

Data Collected by K F Meyer

State	Outbreaks
California	147
Washington	0
Colorado	26
Oregon	21
New York	19
Montana	10
New Mexico	11
Wyoming	8
Idaho	7
Nebraska	6
Tennessee	6
Ohio	5
Illinois	4
Massachusetts	4
Michigan	4
North Dakota	4
Pennsylvania	4
Indiana	3
New Jersey	3
Texas	3
Canada	2
Connecticut	2
South Dakota	2
Utah	2
Wisconsin	2
Alabama	1
Arizona	1
Arkansas	1
Florida	1
Iowa	1
Kansas	1
Maine	1
Minnesota	1
Missouri	1
Oklahoma	1
Virginia	1
West Virginia	1
	367

Home canned products—284 outbreak

Commercially canned products—83 outbreaks

(No outbreaks have occurred from commercially canned products since 1924)

their problems however and solved their difficulties by better methods of packing and processing Since 1924 no cases of botulism have occurred from food canned in American factories

Home canned food products have caused from ten to twenty out breaks a year Faulty methods recommended to home makers by some extension services newspaper bureaus and manufacturers were the cause of much of the trouble When the campaign for home canning was inaugurated during the Second World War faulty methods were discarded and great emphasis placed upon proper preservation of all home canned food products As a result the ex pected increase in botulism did not take place

Table 58.—Foods Involved in 367 Outbreaks of Botulism 1899-1942
Data Collected by K. F. Meyer

Food	Number	Remarks
Vegetables and Fruits		
String beans	83	Three commercially packed
Corn	36	One commercially canned
Spinach or chard	22	Ten commercially packed
Beet tops	17	Two commercially packed
Asparagus	13	Home canned
Olives (minced olives included)	13	Twelve commercially packed
Beans	10	Home canned
Chili peppers	9	Home canned
Peas (?)	8	Home canned
Beet tops	7	Home canned
Figs	6	Home canned
Apricots	4	Home canned
Tomatoe	4	Home canned
Mushroom	3	Home canned
Okra	3	Home canned
Pears	3	Home canned
Okra and beans (1 okra, beans and tomatoes)	2	Home canned
Green tomatoes	2	Home canned
Antipasto (Italian)	1	Commercially packed
Applesauce	1	Home preserved
Apricot butter	1	Home canned
Beans and peppers	1	Home canned
Black eyed Susan beans	1	Home canned
Home brew	1	Home canned
Cauliflower	1	Home canned
Celery	1	Home canned
Eggplant and green pepper	1	Home canned
Mangoes	1	Home canned
Mushroom sauce	1	Commercially prepared
Pawpaw	1	Home canned
Peas, string beans and carrots	2	Home canned
Persimmons	1	Home canned
Pickles	2	Home canned
Pimentos	1	Home canned
Okra, sour grass, tomatoes	1	Home canned
Salad dressing (mustard)	1	Home canned
Shallots, Muscari	1	Commercially packed in Italy
Soybean mash, Natto	1	Home preserved
Squash	1	Home canned
Succotash	1	Home canned
Tomato catsup	1	Commercially packed
Tomato juice	1	Home canned
Tomato relish	1	Home canned
Turnips	1	Home canned
Vegetables	1	Home canned
Vegetable soup mixture	1	Home canned
Meat		
Ham (deviled ham included)	5	One commercially preserved
Sausage	3	Two commercially preserved
Beef	2	Home preserved
Blood sausage	2	Home preserved
Chicken	2	Home preserved
Pork products	2	One commercially packed
Beef tamales	1	
Buffalo meat	1	Home canned
Calf's head vinaigrette	1	Home preserved
Frankfurter sausage	1	Home preserved
Meat and cherries	1	Home canned
Minced meat hamburger	1	Home preserved
Potted meat	1	Commercially canned

Food	Outbreaks	Remarks
Pork and beans	1	Commercially canned
Prepared food (?)	1	
Sausage and string beans	1	Home preserved
Tongue	1	Home preserved
Fish and Sea Foods		
Tuna	7	Three commercially canned
Salmon	7	One commercially canned
Clams (clam juice and broth included)	4	Four commercially canned
Sardines (1 [illegible]ardine and tomato sauce)	3	Three commercially canned
Crab	1	Home canned
Fish (pickled)	1	Home Canned
Herrings	1	Home Preserved
Sprats	1	Commercially canned
Milk and Milk Products		
Cheese	5	Home prepared
Milk (canned)	2	Two commercially canned
Causative food unknown (Symptomatology typical)	33	
Total	367	

PREVENTION AND CONTROL

The prevention of botulism depends on careful and adequate methods of preservation of foods especially home canning All non acid foods (vegetables and meats) should be processed for adequate times and temperatures under steam pressure Only in this manner can the heat resistant spores be destroyed Wherever there is any question about adequacy of process the foods should be thoroughly boiled before serving Foods with appearances of spoilage as characterized by bad odor should not be eaten

Suspected food should be destroyed by adding lye allowing it to stand for 24 hours then burying it in the ground

Antitoxin is available for cure of botulism but is not very successful after symptoms are evident Antitoxin of one type will not protect against the other type

Bivalent antitoxin protecting against both types A and B is available commercially It must be given in large amounts and as early as possible

ITEMS OF NOTE

1 Botulism is caused by the toxin of the botulinum group of bacteria The toxin is ingested in food which has supported the growth of one of the organisms
2 The toxin free cells of this organism are harmless to man and animals in the numbers which would ordinarily be ingested
3 The toxin is quickly destroyed by boiling

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Mangoes	1	Home canned
Mushroom sauce	1	Commercially prepared
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Persimmons	1	Home canned
Pickles	2	Home canned
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Tomato juice	1	Home canned
Tomato relish	1	Home canned
Turnip	1	*Home canned*
Vegetables	1	Home canned
Vegetable soup mixture	1	*Home canned*
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3 The toxin is quickly destroyed by boiling

4 Spores are present in the intestinal tract of certain animals without producing symptoms of illness
5 Spores are widely distributed in nature
6 Prevention of botulism involves careful preservation and handling of foods especially those which are packed in the home

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CHAPTER XXXVI

TETANUS

TETANUS is the result of wound infection with the tetanus organism The disease affects all mammals both man and animal in varying degrees of severity The natural habitat of the organism is the intestine of the herbivorous animals from which it is spread universally To a less degree man likewise acts as an intestinal carrier

Tetanus has been recognized since the time of Hippocrates It has always been a scourge accompanying war In 1885 Nicolaier demonstrated the presence of the infecting organism in garden earth and in 1889 Kitasato isolated it in pure culture

THE ETIOLOGIC AGENT

Clostridium tetani is an anaerobic spore bearing organism of considerable resistance The spores are destroyed by direct sunlight but when protected will remain alive and virulent for years They are not susceptible to the ordinary disinfectants or to boiling water except when exposed over long periods

The distribution of the spores is universal They are present in the soil practically everywhere but are especially abundant in soil fertilized with human or animal excreta

Animals may carry tetanus organisms in their intestines over long periods of time without harm to themselves Noble (1) found 18 per cent of the horses in the vicinity of New Haven so affected The presence of the organisms in the intestine is not always due to constant reinfection for Noble found one horse to harbor the organism continuously for four months although other horses in the same stable were free Apparently the organisms grow and multiply in the intestine and are eliminated in great numbers with the dejecta

According to Park 15 per cent of the horses and calves in the vicinity of New York City harbored tetanus bacilli in their intestines Ninni (3) cultivated the organisms from eight different por

tions of the stomach and intestine in forty two rabbits and guinea pigs with very constant results

Man may carry the organisms in his intestine likewise Pizzini (4) found 5 per cent of human feces to harbor tetanus bacilli Men working around horses and stables however were carriers in about 30 per cent of the instances while men in other occupations showed about 2 2 per cent Tulloch (5) studied the feces of 21 men returned from overseas army service in 1919, obtaining positive results in 33 per cent from 33 civilians in England 16 per cent were positive Ten Broeck and Bauer (6) in 1921 examined the stools of 78 Chinese in Peking and found 34 7 per cent harboring tetanus bacilli in 1924 they examined 539 more such specimens from various parts of China finding 26 5 per cent positive Buzello and Rahmel (7) in Germany found 20 per cent of the feces from 40 individuals positive Van der Reis (8) found tetanus bacilli in practically pure culture in the large intestine of one of his patients Bauer and Meyer (9) studied 487 specimens of human dejecta in California of which 24 6 per cent were positive In addition 43 specimens from 19 other states were examined of which 9 showed tetanus bacilli Sex age and occupation played no part in the distribution of carriers No atoxic strains were found in the 129 cultures isolated

Although the natural habitat of the tetanus bacillus is the intestine of the herbivorous animal (the horse or the cow) spores of the organisms have been found in numerous locations McCoy showed them in hay dust in the mortar of old masonry in the dust from horse hair in the dust in houses barracks and hospitals and in court plaster (10) It is only natural to expect to find such a resistant organism anywhere that the wind might carry the dust of the soil

Gilles (16) studied 63 samples of street dust collected over a wide area in Baltimore as far as possible free from recent contamination with horse manure Eleven samples yielded tetanus bacillus nine of which produced toxin and two no toxin Apparently the elimination of the horse from city streets has not entirely freed street dust from tetanus organisms

Gelatin sold for human consumption may contain numerous spores In Professor Rettger s laboratory in New Haven for several years the stock culture of tetanus for the demonstration of the disease in laboratory animals was a package of household gelatin

THE DISEASE IN ANIMALS

Tetanus whether in man or animals is a wound infection requiring a broken skin for the passage of the organisms By mouth neither the organism nor its toxin is harmful The organism locates in the wound where if anaerobic conditions are present it proceeds to grow and secrete its powerful toxin The organism does not wander far from its portal of entry It has been found in the lymphatics liver and spinal fluid (15) on a few occasions however The toxin invades the nerve tissue for which it has a special affinity thus causing the characteristic symptoms

Among domestic animals the horse is most susceptible to the disease followed by sheep and goats in order Cattle are only slightly susceptible although they may develop the disease upon artificial inoculation Dogs and cats are seldom affected Among the laboratory animals guinea pigs and mice are extremely susceptible but rats and rabbits require larger amounts of material The hen is quite refractory

THE DISEASE IN MAN

The prevalence of the disease in man varies in different localities according to the contamination of the soil with tetanus spores For instance the Hudson River Valley and Long Island show a much higher incidence than do other parts of the country—a fact that coincides with the contamination of the soil

The average death rate from tetanus for the ten year period 1923 to 1932 according to Merkert (17) was 1 28 for 100 000 population for the United States as a whole 1 01 for the State of Minnesota and 0 95 for the City of Minneapolis

The nature of the wound influences the development of the tetanus organism Puncture wounds such as those caused by stepping on a nail are bad Wounds infected with other organisms such as the Welch bacillus favor the development of the tetanus bacillus

Gunshot wounds either from bullets or blank cartridges seem to be especially dangerous The number of cases of tetanus following Fourth of July celebrations some years ago caused the American Medical Association to initiate a campaign in the treatment and care of wounds following accidents from fireworks The deaths fell from 406 in 1903 to zero in 1916 and have remained at a low level since

then In 1937 there were 2 cases of tetanus developing from 7 205 injuries connected with Fourth of July fireworks (18), the low rate being due to immediate use of tetanus antitoxin

Toy pistols were investigated by McIntosh (19) who showed that paper wads were free from tetanus but that felt wads harbored the spores When the skin is accidentally lacerated by the explosion the spores find an ideal medium for development in the lacerated necrotic flesh

Tetanus in American soldiers during the First World War was controlled by the administration of tetanus antitoxin to every wounded man at the dressing station on the battle front at the same time he received the first dressing of his wounds The rate for the American Army in 1917 18 was 1 in 6 224 wounded (36 cases of tetanus in 224 089 war wounds) against the British rate in September 1914 before antitoxin was used of 1 in 111

In the Second World War the disease was controlled by the administration of tetanus toxoid to all personnel Experience in both the British and American armies was very satisfactory

The presence of tetanus spores on the instrument causing the wound is not necessary for infection The clothing and the skin are liable to harbor tetanus spores in greater or less numbers especially around the feet Such organisms are carried into the wound

Tetanus of the operating room has not been unknown especially in operations of the abdomen More serious however is tetanus following childbirth a problem giving much concern to obstetricians Tetanus of the new born—trismus neonatorum—is a very common cause of death in the tropics Infection takes place by way of the umbilical cord

Rare cases of tetanus occur with no apparent lesion Several theories have been advanced for this Spores may lie dormant in wound or scar tissue for months or years until released to proliferate and produce toxin They may be inhaled with street dust where they enter the body through the inflamed tissue of the respiratory tract or slight lesions of the nose They may be carried in a dormant condition to the lymph glands liver or other parts of the body where they eventually cause the disease

Biological products in the past have been known to carry tetanus spores and cause the disease when applied In India in 1902 there were 19 deaths following the administration of Haffkines plague vaccine to 107 persons The tetanus bacillus was apparently present

wıth the plague bacıllus growıng ın symbıosıs with ıt and thus pro ducıng toxın

In 1901 ın St Louıs seven chıldren dıed from tetanus following the admınıstratıon of dıphtherıa antıtoxın The serum ın thıs ın stance was sterıle but the horse from whıch the serum had been withdrawn was ın the ıncubatıon stage of tetanus and thus carrıed ın ıts blood stream a large amount of tetanus toxın (11)

Smallpox vaccıne was occasıonally contamınated with tetanus spores ın the days before governmental supervısıon On July 1 1902 all vaccıne virus as well as other bıologıcs sold ın ınterstate traffic ın the Unıted States was requıred to come from a manufacturıng plant lıcensed by the Unıted States Publıc Health Service Elaborate precautıons agaınst and tests for tetanus sınce then have been com pulsory makıng ıt ımpossıble for materıal so contamınated to find ıts way ınto the market

Anderson (12) studıed all the cases of tetanus developıng after vaccınatıon between 1904 and 1915 Forty one such ınstances had occurred but not once could tetanus spores be found ın the virus ın the same stock as that used for vaccınatıon A study of commercıal vaccıne virus suffıcıent to vaccınate 200 000 people showed no ındı catıon of the presence of tetanus organısms Among 385 000 men vaccınated ın the Unıted States Army 6 cases of tetanus developed none whıch had any relatıon to the vaccıne vırus Among 200 000 persons vaccınated ın the Unıted States Navy two developed teta nus neıther of whıch cases had any relatıon to the vaccıne vırus The causes for such cases are several such as uncleanlıness accı dental removal of the scab bunıon pads etc (see chapter XI)

Infectıon of a wound wıth the tetanus organısm followed by growth and the productıon of toxın ın the wound does not always result ın a case of tetanus Some straıns of tetanus bacıllı produce toxın of such a low grade that ıt has no effect upon the body Natu ral ımmunıty ıs exhıbıted by some persons due to tetanus antıtoxın ın the blood stream Accordıng to Ten Broeck and Bauer (13) antı toxın ın the blood stream ıs correlated wıth the tetanus organısm ın the dıgestive tract Twenty sıx persons who exhıbıted antıtoxın lıke wıse were ıntestınal carrıers while 36 persons who exhıbıted no antıtoxın were free from the organısm ın the ıntestıne (wıth only two exceptıons)

Mortalıty from tetanus ınfectıon depends upon the care which the case has receıved Before the ıntroductıon of tetanus antıtoxın

the mortality was about 85 per cent (14) In the British Army during the First World War 2,152 soldiers developed the disease, of which 1 011 died—47 per cent However, among 715 who received no antitoxin or who exhibited a very short incubation period and received antitoxin in France the death rate was 71 2 per cent while among 1,437 men treated with antitoxin in England the death rate was only 34 8 per cent

Cases of tetanus which have received no antitoxin until after symptoms have developed do not have as great a chance for recovery In Minnesota Merkert (17) reported a mortality of 63 6 per cent in 33 cases from 1923 to 1932 In New Orleans (20) Gessner reported 70 per cent mortality in 368 cases from 1906 to 1918 Graffagnino and Davidson 67 4 per cent in 596 cases from 1918 to 1923 Graves 52 per cent in 217 cases from 1923 to 1930 Boyce and McFetridge 59 5 per cent in 185 cases from 1929 to 1934 Cases of tetanus in a group of hospitals in half a dozen cities were studied by Huntington Thompson and Gordon (21) with 63 per cent mortality in 642 cases In Boston at the Massachusetts General Hospital the mortality was 69 9 per cent in 116 cases from 1872 to 1921 it was 45 5 per cent in 33 cases from 1922 to 1933

The longer the incubation period the better are the chances of the patient s recovery the sooner the patient receives antitoxin the better are his chances also

PREVENTION

The prevention of tetanus depends upon the administration of antitoxin as soon as after infliction of the wound as convenient but in any case before the organism has had a chance to proliferate in the tissue and toxin fixation of the nerve tissue has occurred

Antitoxin gives only a passive immunity however and so it has certain disadvantages Toxoid has come into use for active immunization of those groups especially exposed to infection Satisfactory results have been obtained in both the British (23) and the American Armies (24) Penicillin added to antitoxin has been used for treatment of the disease

ITEMS OF NOTE

1 *The natural habitat of the tetanus organism is the intestine of the herbivorous animals (horse and cow)*
2 Man may carry the tetanus organism in his intestine without harm to himself

3 Tetanus organisms and tetanus toxin by mouth are harmless
4 Tetanus is a wound disease requiring a broken skin for entry
5 Tetanus spores are distributed universally They are much more abundant in highly fertilized soil
6 Tetanus organisms do not ordinarily multiply outside the animal body
7 The incidence of tetanus in man is correlated with the contamination of the soil with spores
8 The cure of tetanus by use of antitoxin is not entirely satisfactory nearly half the cases dying Antitoxin when used should be administered as soon as possible after infliction of the wound Penicillin added to antitoxin has been used for cure of the disease
9 The prevention of tetanus by use of toxoid is quite certain

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the mortality was about 85 per cent (14) In the British Army during the First World War 2 152 soldiers developed the disease of which 1 011 died—47 per cent However among 715 who received no antitoxin or who exhibited a very short incubation period and received antitoxin in France the death rate was 71 2 per cent while among 1 437 men treated with antitoxin in England the death rate was only 34 8 per cent

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2 Man may carry the tetanus organism in his intestine without harm to himself

Type B Associated with lamb dysentery

Type C Associated with struck in sheep

Type D Associated with enterotoxemia of sheep

Besides certain cultural differences all four types produce powerful toxins which are distinct from each other The antitoxins of each type will neutralize the toxin of some of the other types

Morphologically all types are similar They are 1 0 to 1 5 μ wide by 4 0 to 8 0 μ long They occur singly or in pairs and occasionally in long threads or chains Capsules are present on specimens taken directly from the animal body They are non motile Spores when present are oval central or excentric very often specimens from the animal body will not show spores however

Clostridium novyi (*Clostridium oedematiens*) was isolated in 1894 by Novy (18) from a guinea pig Weinberg and Seguin (4) described it as a new species when they isolated it from a human case during the First World War It is 0 8 by 1 0 broad and 4 to 5 μ long with rounded ends occurring singly or in pairs and is somewhat motile It is a strict anaerobe growing with great difficulty and forming abundant central or subterminal spores It produces an active soluble toxin which is virulent for all laboratory animals

All these organisms are found in the soil Normal animals carry most of them in the intestine *Clostridium perfringens* type A seems to be especially widespread Taylor and Gordon (17) and others have found it in the intestinal canal of normal cattle sheep pigs dogs cats rabbits guinea pigs poultry and man Maes (16) demonstrated that woolen cloth carried large numbers of anaerobic spore forming gas producing bacilli morphologically resembling the Clostridium group

THE AFFECTION IN ANIMALS

Wound infections of animals with members of the gas gangrene group are known as malignant edema The horse is most susceptible the affection appearing as a complication of surgical or accidental wounds Sheep are often affected after castration or wound inflicted while shearing Cattle are not as susceptible to the disease but occasionally develop it following parturition Dogs sometimes are infected through wounds inflicted while fighting Guinea pigs rabbits mice etc are very susceptible to injection of any of these organisms The affection in animals is characterized by a hot painful crepitating swelling at the point of inoculation The outcome is usu

CHAPTER XXXVII

GAS GANGRENE

GAS GANGRENE in man is caused by the invasion into injured tissues of certain anaerobic spore forming organisms belonging to the group of which the Welch bacillus is a member These organisms are frequently found in the intestinal canal of normal animals where they lead a saphrophytic existence

THE ETIOLOGIC AGENTS

A large number of anaerobic spore forming bacilli have been described as the cause of gas gangrene In some instances different names have been used for the same organism at other times the organism was only an incidental invader and was not responsible for the gangrenous condition Reed and Orr (18) list 21 members of the group associated with the disease

Clostridium septicum (Vibrion septique Clostridium edemitis maligni) was discovered by Pasteur (3) in 1877 associated with infections of animals which were supposed to have died of anthrax Koch and Gaffkey later isolated the organism and studied it carefully It is considered that Bacillus III of von Hibler and the bacillus of Ghon and Sachs are identical with it The bacillus is 0 8 to 1 0 μ broad by 2 to 10 μ or more long occurring principally in long chains The spores are oval and excentric and are very resistant The bacillus is motile and does not form a capsule It produces a powerful exotoxin

Clostridium perfringens (Clostridium welchii, Bacillus aerogenes capsulatus Bacillus phlegmonis emphysematosae) is the Welch bacillus isolated by Welch and Nuttall (2) in 1892 in an autopsy of a cadaver which showed gas bubbles in the blood vessels There are four toxicogenic types which have been encountered

Type A Present in human infections Not found in animal infections

the type of anaerobe present in order that the correct specific serum may be given and later in the disease to determine the number of organisms present in order that closure of the wound may be per formed with intelligence

Reports of gas gangrene infections are increasing in civil life whether actually or from better diagnosis it is difficult to state Ghormley (8) found that compound fractures produced the largest number of cases of this trouble Reeves (11) experienced most cases in patients past 50 years of age who were constitutionally below normal especially those with circulatory failure arteriosclerosis thrombo angitis obliterans and diabetes mellitus

Callander (12) lists among the varieties of trauma that predispose to gas gangrene crushing and lacerating accidents particularly com pound fractures where street and farm dirt gain access to injured muscles gunshot wounds and puncture wounds where mud gravel or bits of cloth are carried into the tissue and injuries to the gluteal and peroneal regions where fecal contamination may occur

Aerobic organisms such as streptococci and staphylococci are usually found in wounds in symbiosis with the anaerobes and pro duce toxins within the tissues which create conditions favorable to the growth and pathogenic action of the anaerobes

The Welch bacillus is most often encountered in civil life very often other anaerobes being absent Some strains of the Welch ba cillus are not pathogenic however but give rise to exotoxins which enhance the virulent character of any other anaerobes that may be present

Mortality is about 50 per cent under ordinary conditions In World War I it was 48 5 per cent in the American Expeditionary Force in France in civil life it was 49 7 per cent in 607 cases col lected by Millar (13) up to 1930 in cases following amputation for diabetic gangrene it was 75 per cent according to Eliason (14) In World War II it was reduced to 11 per cent (20)

TREATMENT AND PREVENTION

Mortality is considerably reduced by antitoxin Ghormley states that at the Mayo Clinic 33 cases were encountered in a five year period mortality was 44 5 per cent in the group without antitoxin 13 4 per cent in the group receiving antitoxin Bates (9) reported 16 cases treated without antitoxin showed a mortality of 50 per cent while 16 cases treated with antitoxin had a mortality of 18 per cent

ally fatal Large numbers of gas bubbles are found on post mortem examination in the subcutaneous tissue surrounding the point of infection *Cl novyi* causes black disease in sheep in various countries of the world The sheep liver fluke is probably responsible for the spread of the disease

Infection by ingestion causes serious damage in sheep and lambs *Cl septicum* produces a disease known as braxy' or 'bradsot in the Scandinavian countries *Cl perfringens* type B causes lamb dysentery in the British Isles and northwestern United States The toxin forms in the intestine Struck is caused by type C of this organism It is found in England and Wales Enterotoxemia is a condition of sheep caused by *Cl perfringens* type D It occurs in the United States Australia and Wales

THE DISEASE IN MAN

Gas gangrene in man is a war time affliction Soils heavily fertilized with animal or human excreta contain numerous spores of the offending organisms with which gunshot wounds become contaminated The depth of the wound as well as the introduction of other organisms influence the extent of the resulting edema The site of the wound influences to some extent the chances of infection The buttock and the thigh are more apt to show gas gangrene when wounded than other parts of the body (20)

At the site of the wound an extensive hemorrhagic edema of the subcutaneous tissue develops the serous effusion from which is frothy with gas production and has a foul odor

Taylor (6) has classified the various stages in the course of gangrene as follows 1 dormant stage 2 stage of acute gaseous distention 3 explosive stage 4 stage of systemic intoxication and 5 stage of septicemia

Christopher (7) states that there is no single pathognomonic clinical sign *or symptom of gas gangrene The condition is a syndrome* and the diagnosis generally depends on the combined presence of several signs or symptoms He gives the more reliable factors in diagnosis as history of recent wound swelling increased frequency of pulse rate tympany crepitus pale color of skin odor ability to milk gas bubbles out of wound thin discharge roentgenographic findings and maintained intelligence of the patient

The laboratory may be of assistance in making bacteriological examinations of an open wound early in the disease to determine

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Eliot and Easton (10) had a mortality rate of 20 per cent in cases where antitoxin was used Eliason reduced the mortality from 49 per cent to 25 per cent The earlier the antitoxin is administered the better chance does the patient have for recovery Polyvalent types of antitoxin (Welch bacillus and *Cl septicum*) are recommended Treatment with antitoxin must be combined with surgical pro cedures however, if the best results are to be expected

Roentgen treatment of gas gangrene has been recommended by Kelly and his co workers (15) In their experience there was no mortality when patients were treated in the first 24 hours

The sulfonamides have been of value in some instances and have proved disappointing in other cases in the treatment of the disease Penicillin when used in conjunction with surgery and antitoxin has proved of value (20)

Cl perfringens toxoid has been administered with tetanus toxoid with indications of success (19)

ITEMS OF NOTE

1 Gas gangrene is an affection of man caused by certain anaerobic spore forming organisms
2 The more important organisms are *Clostridium septicum Clostridium perfringens* and *Clostridium novyi*
3 The organisms are found in the intestines of many animals as well as of man
4 Infection of man takes place by way of wounded tissue
5 Malignant edema in animals is caused in a similar way by the same group of organisms
6 The prevention of the disease rests upon the cleanliness of wounds
7 The cure of the disease rests upon surgery together with the specific antitoxin and other means of therapy

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SECTION FIVE

A REVIEW OF THE ROLE PLAYED BY EACH ANIMAL IN THE SPREAD OF DISEASE

CHAPTER XXXVIII

THE ROLE OF DIFFERENT ANIMALS AND BIRDS IN DISEASES TRANSMITTED TO MAN

THE progress of man from cave shelter to pent house has been influenced constantly by the lower animals It is human nature to take credit for all desirable attainments to refuse responsibility for the undesirable Man can pride himself therefore on the wisdom of his ancestors going back as far as the stone age who brought under domestication various animals But for that he would be living under conditions which he passed some thousands of years ago for no people have advanced very far who have not made use of domestic animals Because of that his ascent from a savage state was hastened—he was assured both bountiful larder and plentiful labor the excess food supply not required for home use was a source of barter and the emancipation for the heaviest burdens of labor allowed time and energy for trade commerce and travel That was only the beginning however Animals proceeded to change the frontiers of nations to crown and uncrown kings to dictate religious practices and to cause many a diplomatic headache they have left a mark on architecture on landscapes on styles of clothes they have sent to death untold millions of people and have saved from death other millions

THE HORSE

The horse is counted among the most intelligent of the lower animals His friendship for man has been close and his contact intimate yet the instances when he has conveyed a communicable disease to his master have been comparatively rare (table 59)

The horse was domesticated at a relatively recent date but it immediately took a leading role in the destinies of mankind No other animal has so fired the imagination There have been demon

time went on horses made it possible for armies to carry with them food supplies ammunition and even heavy cannon which otherwise would have been left behind

The horse has had an even more important part to play in the development of civilization from a non military standpoint The wagons of commerce the carriages of society the messengers of mercy and love all depended upon the horse man s faithful servant and friend

The number of horses in the United States has been diminishing during the last few years with the increased use of motor transpor tation In 1918 there were 21 555 000 horses in the country while in 1927 there were 15 279 000 and in 1940 only 10 087 000 The con trol of contagion in horses has been made easier not only by the lessened number of such animals but also by the fact that they have almost disappeared from city streets The horses that remain are largely on the farms where they lead lives more or less isolated from other animals of their kind and hence have less opportunity than in previous times of contracting contagion

Glanders is the only disease which is distinctly of an equine na ture the horse being the only reservoir There never were very many human infections and now the disease has been eradicated in the United States and Canada Equine encephalomyelitis is serious in epidemic seasons but domestic fowls and other birds are of more consequence than horses as reservoirs of infection Anthrax is some times communicated to man from infected hides or from horse hair used in shaving brushes but such cases are not numerous Brucello sis is an important disease in horses causing their non use due to fistula of the withers Horses however are relatively unimportant sources of human infection compared with the other animals Horses suffer from such skin infections as histoplasmosis sporotrichosis and ringworm but the number of human infections acquired from this source is not large

Horses are resistant for the most part to the rodent diseases al though in Panama they have been found to harbor the spirochetes of endemic relapsing fever Ticks of the *Dermacentor* variety feed on horses and persons pulling off such ticks and accidentally crush ing them in their fingers expose themselves to tularemia or Rocky Mountain spotted fever

A few cases of Salmonella food poisoning have arisen from con sumption of horse meat in Europe Tuberculosis (bovine type) may

horses angel horses ghost horses witch horses fairy horses sun horses moon horses wind horses sea horses night horses and headless horses The centaur of the early Greeks that weird combination of a horse with a man s body at its head resulted from impressions formed by the first encounters of Greek warriors with an enemy mounted on horses The American Indians also believed that horse and rider were one being when they first met mounted Spanish soldiers Horses have been worshipped in various lands The Trojan horse was accepted by the people of Troy because they thought the Greeks had built it as a peace offering to the Goddess Athena

The horse has left a more complete record over the earth for a longer period of time than any other of the domestic animals Some millions of years ago it was a dog like creature with five toes Fossil remains would indicate that it roamed pretty well over the earth including America By the time that man took his place in the scheme of things perhaps a hundred thousand years ago it had reached its final state of development the equus form that we know today Its range by then was confined to the plains of Asia north of the Caspian sea and eastward to Mongolia Primitive man used the horse only as a source of food supply In the late stone age period about 25 000 years ago horses must have been quite plentiful for one camp site of less than two acres in France has shown the bones of more than eighty thousand horses Through the centuries that followed drawings of horses were made on the walls of caves but always indicating the animal in a wild state The strength the speed and the sagacity of the beast made it difficult to capture and domesticate

The period known as civilization was ushered in as a horseless age Babylonia in all its wisdom owned no horses Egypt had no horses with which to build the pyramids and none for several hundred years to come the Arabs did not use horses until after the Christian era *Horses were first introduced as servants of man by* the wild tribes living in the hills of Persia About four thousand years ago these tribes descended to the plains of Mesopotamia raiding the settlements and driving out the Sumerians and Babylonians The progress of the invaders was greatly facilitated by the asses of the east so called by the dismayed Babylonians

The horse has held a significant place in military operations At first it was used to draw war chariots for it was a small animal By 750 B C breeds had been developed large enough to carry riders As

heaval the first consideration of health officers is to the milk supply that children and the sick may not suffer

In 1940 there were 60 675 000 head of cattle (three months old or over) in the United States of which number 33 523 000 were milk cows The same year there were slaughtered 19 756 000 cattle and 5 390 000 calves at federally inspected establishments while 5 215,000 cattle and 3 731 000 calves were slaughtered at other establishments

More than a score of diseases may be transmitted from the cow to man (table 60) Bovine tuberculosis once so common has been practically eliminated in the United States Brucellosis is a serious problem *Brucella abortus* has a relatively low pathogenicity for man but the hog and goat strains of the organism cause serious infection when they are present in milk Pasteurization is an adequate safeguard for milk and proper cooking for meat Slaughter house workers are subject to Brucella infection by contact Salmonella food poisoning may be caused by infected meat the cow being susceptible to several Salmonella types Anthrax may be contracted by persons handling infected hides Listerellosis is an encephalitis of cattle which sometimes infects man

Several virus diseases are of importance Cowpox is contracted directly from the cow but in the United States it is rare except as the virus is propagated for vaccine to be used for smallpox immunization Sometimes cows are infected with cowpox by persons who have been recently vaccinated Milkers nodules occur in persons who have been associated with cattle suffering from this infection Foot and mouth disease occasionally infests man but outbreaks in cattle in the United States are rare Rift Valley fever is found only in Africa Cattle suffer from rabies and the virus is present in the milk and tissues several days before symptoms appear but human infections from these sources are rare Scours (pneumo enteritis) of cattle is caused by a filtrable virus according to Baker (3) and this virus is possibly the same as the one isolated by Reimon Price and Hodges (4) in virus dysentery of man Q fever is a rickettsial disease from which cattle suffer slaughter house workers being especially liable to infection

The fungous infections which affect cattle are not of great importance Coccidioidomycosis is a serious disease in man but other sources of infection than cattle may be more important Actinomycosis is common in cattle but the method of human infection is in

be contracted by horses from cattle and such infected horses may serve as reservoirs for the reinfection of cattle but rarely of man

The horse suffers from a variety of animal parasites (Monnig lists thirty nine helminths) but none are of significance to man in the United States

Table 59 —DISEASES TRANSMITTED FROM HORSE TO MAN

DISEASE	ETIOLOGIC AGENT	METHOD OF HUMAN INFECTION
Anthrax	*Bacillus anthracis*	By contact hair and hide
Brucellosis	*Brucella abortus Brucella suis*	By contact
Encephalitis St Louis type	Filtrable virus	By mosquito bite
Encephalomyelitis equine	Filtrable virus	By mosquito bite
Glanders	*Malleomyces mallei*	By contact
Histoplasmosis	*Histoplasma capsulatum*	By contact
Relapsing fever (endemic type)	Spirochetes genus *Borrelia*	By tick bite
Ringworm	*Tinea barbae* *Tinea circinata*	By contact
Sporotrichosis	*Sporotrichum schenckii*	Through skin abrasions
Tuberculosis	*Mycobacterium tuberculosis* var *bovis*	Through infection of cows

THE COW

The cow has been called the foster mother of the world —it is the most indispensable of all the domestic creatures furnishing not only *labor but milk and meat as well it has also been called a pest* to be found wherever civilized man makes his abode —it is a prolific source of contagious diseases for man

Cattle were domesticated in very early times first in Asia from whence they migrated into Africa and then to Europe There were several wild types which eventually served to produce the various breeds known today Cattle have taken a spectacular place in the history of the world From time to time they have held temporary prominence as sacred animals—the Bible reports golden images of calves which the Israelites worshipped a stone statue of a sacred cow has been found in Egypt the stone bull of Siva is still held in reverence in India They have furnished amusement and sport in the arenas of Spain and the rodeos of the United States always however with man as the opposing contestant and the animal as the eventual loser For the most part cattle have held a lowly place content to pull a farm cart or furnish milk or wait for the butcher

Present day civilization is absolutely dependent upon cattle for both milk and meat In times of storm violence or economic up

Several score of animal parasites are found in cattle The only ones of importance in the United States are the beef tapeworm and the hydatid tapeworm *Echinococcus granulosus* Neither of the flukes *Fasciola hepatica* or *Schistosoma japonicum* are found in this country The round worms found in cattle sometimes afflict man in other countries They include the guinea worm *Dracunculus medinensis* the sheep wireworm *Haemonchus contortus* a throat worm *Syngamus laryngeus* and an intestinal parasite *Trichostrongylus* African trypanosomiasis is a protozoan infection not found elsewhere than certain parts of Africa

THE HOG

Swine have been used for food since early times In Turkestan bones of swine were found in camp litter dating about 6000 B C in China swine were supposed to have been domesticated in 3468 B C

The number of hogs four months old on farms in the United States April 1 1940 was 34 037 000 The same year 50 398 000 were slaughtered at establishments under federal inspection and 27,212 000 at other establishments

Hogs do not have the intimate contact of the home in the United States that they have in some countries hence the opportunity to transmit infection (as well as to contract it from the household) is lessened Furthermore the relatively short life of the pig before it is slaughtered lessens opportunity for it to develop many diseases Swine are responsible for a considerable number of human infections however

There are five bacterial diseases of importance which are transmitted to man (table 61) Anthrax is acquired usually by handling the hides and bristles Brucellosis is acquired by contact the persons most in danger being butchers and abattoir workers *Brucella suis* and *Brucella melitensis* infect hogs but not *Brucella abortus* Salmonella food infections from pork and pork products are not common Hogs are susceptible to many types of the Salmonella organism but not to *Salmonella typhimurium* Swine erysipelas is of economic importance but human infections are often acquired in other ways than by contact with hogs Tuberculosis of the human type may be contracted by hogs from garbage contaminated by a tuberculous person All such garbage fed to hogs should be cooked Bovine tuberculosis may also be contracted by hogs from infected cattle Tuberculous hogs ars eliminated by inspection at slaughter

doubt Ringworm especially *Tinea barbae* and *Tinea circinata* occasionally may be contracted by man from contact with cattle

Table 60 —DISEASES TRANSMITTED FROM COW TO MAN

DISEASE	ETIOLOGIC AGENT	METHOD OF HUMAN INFECTION
Actinomycosis	*Actinomyces bovis*	Method in doubt
Anthrax	*Bacillus anthracis*	By contact and hides
Brucellosis	*Brucella abortus* *Brucella melitensis* *Brucella suis*	From milk and by contact
Coccidioidomycosis	*Coccidioides immitis*	By inhalation and through abrasions
Cowpox	Filtrable virus	Through skin abrasions and vaccination
Diphtheria	*Corynebacterium diphtheriae*	From milk
Foot and mouth Disease	Filtrable virus	By contact and through milk
Listerellosis	*Listerella monocytogenes*	Method uncertain
Milkers nodules	Probably a virus	By contact
Milk Sickness	A chemical poison	From milk
Q Fever	*Rickettsia burneti*	By tick bite
Rift Valley fever	Filtrable virus	By mosquito bite
Ringworm	*Tinea barbae* *Tinea circinata*	By contact
Salmonella food poisoning	*Salmonella* bacteria	From meat
Scarlet fever	*Streptococcus pyogenes*	From milk
Septic sore throat	*Streptococcus pyogenes*	From milk
Tuberculosis	*Mycobacterium tuberculosis* var *bovis*	From milk or meat
Animal Parasites		
Beef tapeworm infection	*Taenia saginata*	From meat
Fascioliasis	*Fasciola hepatica*	From raw plant food
Dracontiasis	*Dracunculus medinensis*	From drinking water
Congylonema infection	*Gongylonema pulchrum*	From drinking water
Hydatid disease	*Echinococcus granulosus*	Usually from dog
Lungworm infection	*Metastrongylus elongatus*	By mouth
Sarcocystiasis	*Sarcocystis* species	From contaminated food and water
Schistosomiasis	*Schistosoma japonicum*	Through the skin
Sheep wireworm infection	*Haemonchus contortus*	From drinking water
Syngamus infection	*Syngamus laryngeus*	By mouth
Trichostrongylus infection	*Trichostrongylus* species	From food or water
Trypanosomiasis (African)	*Trypanosoma gambiense* *Trypanosoma rhodesiense*	By tsetse fly bite

Milk sickness is due to a chemical poison found in the milk of cattle which have eaten white snake root People in rural communities may be poisoned but in cities the dilution of the poison with milk from other sources renders milk harmless

Three diseases of human origin diphtheria scarlet fever and septic sore throat are sometimes passed to the cow by an infected milker Many serious epidemics have resulted Pasteurization is an adequate safeguard

six months old) on the farms In the same year 17 351 000 were slaughtered at establishments under federal supervision and 4 232 000 at other establishments

Sheep in their relation to public health are of minor significance (table 62) Anthrax may be contracted by persons handling infected

Table 62 —Diseases Transmitted from Sheep to Man

Disease	Etiologic Agent	Method of Human Infection
Anthrax	*Bacillus anthracis*	From hide and wool
Brucellosis	*Brucella abortus*	
	Brucella melitensis	
	Brucella suis	By contact
Coccidioidomycosis	*Coccidioides immitis*	By inhalation and through abrasions
Foot and mouth disease	Filtrable virus	By contact
Listerellosis	*Listerella monocytogenes*	Method uncertain
Louping ill	Filtrable virus	Method uncertain
Q fever	*Rickettsia burneti*	By tick bite
Rift Valley fever	Filtrable virus	By mosquito bite
Salmonella food poisoning	Salmonella bacteria	*From mutton*
Sore mouth of sheep (contagious ecthyma)	Filtrable virus	Probably through skin abrasions
Rocky Mountain spotted fever	*Rickettsia rickettsi*	By tick bite
Tularemia	*Pasteurella tularensis*	By tick bite
Animal Parasites		
Fascioliosis	*Fasciola hepatica*	From raw plant foods
Lungworm infection	*Metastrongylus elongatus*	By mouth
Hydatid disease	*Echinococcus granulosus*	Usually from dogs
Sheep wireworm infection	*Haemonchus contortus*	From drinking water
Trichostrongylus infection	*Trichostrongylus* species	From food or water
Trypanosomiasis (African)	*Trypanosoma gambiense*	
	Trypanosoma rhodesiense	By tsetse fly bite

hides or wool Listerellosis is not uncommon in sheep but human infections are rather rare Sheep rank close to goats in susceptibility to brucellosis human infections occurring from contact or in slaughtering infected animals Salmonella food poisoning occasionally comes from eating mutton but not as often as from other causes Rocky Mountain spotted fever and tularemia are both found in sheep along with other animals and people bitten by wood ticks or pulling the ticks from the wool and crushing them in their fingers may be infected Foot and mouth disease louping ill and sore mouth in sheep cause human disease very rarely Rift Valley fever is of consequence only in British East Africa Rabies occurs in sheep and persons handling such animals could be infected but this seldom occurs Sheep handlers have suffered from Q fever but it is not certain whether the sheep were responsible or the ticks with which

houses under federal supervision but numerous hogs are slaughtered on farms from which human infections may arise

Table 61 —DISEASES TRANSMITTED FROM HOG TO MAN

DISEASE	ETIOLOGIC AGENT	METHOD OF HUMAN INFECTION
Brucellosis	*Brucella melitensis* *Brucella suis*	By contact and through abrasions
Listerellosis	*Listerella monocytogenes*	Method uncertain
Salmonella food infection	*Salmonella* bacteria	From pork products
Swine erysipelas	*Erysipelothrix rhusiopathiae*	Through skin abrasions
Tuberculosis	*Mycobacterium tuberculosis* var *bovis*	From pork products
	Mycobacterium tuberculosis var *hominis*	From pork products
Animal Parasites		
Amphistomiasis	*Amphistoma hominis*	From food and water
Balantidiasis	*Balantidium coli*	From food and water
Fasciolopsis infection	*Fasciolopsis buski*	From raw plant food
Lung fluke disease	*Paragonimus westermani*	From eating crayfish and crabs
Lungworm infection	*Metastrongylus elongatus*	By mouth from earthworms
Hydatid disease	*Echinococcus granulosus*	Usually from dog
Gongylonema infection	*Gongylonema pulchrum*	From drinking water
Opisthorchiasis	*Clonorchis sinensis*	From eating raw fish
Pork tapeworm infection	*Taenia solium*	From pork
Trichinosis	*Trichinella spiralis*	From pork

Several diseases which may afflict hogs are of lesser importance to man Listerellosis occasionally is found in hogs but human infections are rare Actinomycosis is probably but a slight menace The virus diseases are without significance although hogs are susceptible to foot and mouth disease when exposed

The animal parasites because of the nature of the hog are numerous Among twenty four helminths listed by Monnig (1) which infect hogs nine are transmitted to man Trichinosis is the most serious This together with the pork tapeworm have probably influenced the course of man s actions for thirty centuries They may have been responsible in part at least for the ancient Jewish prohibition against pork The pork tapeworm is of less consequence in the United States but trichinosis infects nearly twenty per cent of the population The other animal parasites which infect hog and man are rare or absent in the United States

THE SHEEP AND THE GOAT

Sheep raising is one of the oldest agricultural pursuits In the United States in 1940 there were 40 129 000 sheep and lambs (over

as they do today they were put into treadmills turning the wheels of industry they were sources of entertainment baiting the bull and the bear or fighting with each other in the pit To fulfill the requirements of these various activities the different breeds have been developed

The number of dogs in the United States is impossible to estimate definitely for many owners have failed to register their animals There are numerous dogs however which can boast no master but wander from the hospitality of one kindhearted person to another or else live on the scraps of the street and garbage pail a menace not only to all other dogs but to mankind as well

Rabies is the most serious of the afflictions which can be charged against the dog In no other animal does the disease find a reservoir for its perpetuation and seldom do other animals spread it farther than one remove" from the dog The increased number of dogs together with rapid modes of transportation of both man and his dog has resulted in a sharp increase in rabies not only in the United States but many other countries Leptospirosis is becoming an increasing problem in dogs with human infections by both *Leptospira icterohemorrhagiae* and *Leptospira canicola*

Tularemia is sometimes found in dogs human infections resulting from contact or from tick bites Brucellosis is occasionally present but the dog is not a large factor in the epidemiology of the disease Coccidioidomycosis by inhalation or through skin abrasion as well as ringworm and sporotrichosis through skin abrasions may be contracted by man from the dog Among the rickettsial diseases the dog is one of the reservoirs of Rocky Mountain spotted fever in the United States and of Boutonneuse fever Brazilian typhus and Kenya typhus elsewhere

Dogs may become infected with various other bacterial diseases from other animals but do not form a serious menace to man Tuberculosis is contracted sometimes from association with tuberculous persons from drinking infected cow s milk or from the offal of slaughter houses Anthrax and glanders are occasionally acquired by dogs from eating animals that have died of those diseases Infection with foot and mouth disease is difficult as is also trichinosis Dogs are sometimes infected with the virus of lymphocytic choriomeningitis They may act as mechanical carriers of rat bite fever where infection has followed the bite of a dog which had recently fed on an animal dead of the disease

the sheep were infested Tuberculosis of bovine or avian origin is sometimes found in sheep, but rarely the human type of disease

Several score of animal parasites infect sheep, few of which find residence in man Several round worms more or less akin to hook worms are found in the United States They are the lungworm and *Metastrongylus elongatus* the sheep wireworm *Haemonchus con tortus* and intestinal parasites of the *Trichostrongylus* species hu man infections are not common The liver fluke *Fasciola hepatica* and the protozoan parasites of African sleeping sickness *Trypano soma gambiense* and *T rhodesiense* are found only in other parts of the world

Goats are very much in the same category with sheep in regard to the public health, with the exception of brucellosis Since goat s milk is used for human consumption, this disease is of importance Without showing any signs of infection goats may excrete thou sands of *Brucella melitensis* organisms in the milk In the warm *countries around the Mediterranean Sea brucellosis has been a seri* ous problem but in the United States the number of goats used for milk purposes is relatively small There have been serious outbreaks however in this country from this source Pasteurization is a safe guard

Goats are rather susceptible to the bovine type of tuberculosis and may infect man through unpasteurized goat s milk or may spread the disease to cattle with which they may be associated

THE DOG

Dogs enjoy a more intimate contact with man than any other ani mal *sharing not only his dwelling but sometimes even his bed and* his board Thus man is exposed to several diseases from which dogs suffer

The dog was the first animal to become domesticated probably some 60 000 years ago by savage cave men and for the same reason that the society matron of today owns a dog—namely the desire of the human being for a pet The early dogs were half wild wolves or jackals which developed rather rapidly through domestication and crossbreeding They adapted themselves quite readily to purposes of economic usefulness They were natural hunters assisting in pro curement of a food supply they were trained to protect other do mestic animals *tending the flocks and herds in agricultural com* munities they were hitched to harness pulling wagon or sled even

helminths being recorded by Monnig Comparatively few of them are responsible for human infection however

Several protozoa infect dogs but are of small epidemiological significance in the United States *Endamoeba histolytica* is sometimes found *Leishmania donovani* and *L tropica* are acquired by dogs but not in the United States *Trypanosoma cruzi* is spread by the dog together with other animals in South America

The dog tapeworm is acquired by man from dogs through swallowing an infected flea while the fish tapeworm comes indirectly from dogs by eating fish which have lived in water contaminated by dog feces *Echinococcus granulosus* is another tapeworm acquired directly from dogs by swallowing dog s feces from soiled fingers All three tapeworms are found in the United States

The flukes are not of importance in the United States Elsewhere in the world they infect dogs incidentally in the same manner as man is infected Dogs may be of importance in passing the parasites back again to fish and crabs however The liver flukes *Clonorchis sinensis* and *Opisthorchis felineus* as well as the intestinal flukes *Echinostoma ilocanum Heterophyes heterophyes* and *Fasciolopsis buski* (reported in dogs only once) are acquired from eating infected fish The lung fluke *Paragonimus westermani* comes from infected crayfish and crabs while the blood fluke *Schistosoma japonicum* passes directly through the skin from water in which it is swimming

Creeping eruption is found in southeastern United States It is caused by the round worm *Ancylostoma braziliense* closely related to the hookworms It passes directly through the skin hence dogs should be kept from bathing beaches where people go barefoot The human hookworm *Necator americanus* is rarely found in dogs while the dog hookworm *Ancylostoma caninum* is seldom if ever found in man The guinea worm *Dracunculus medinensis* parasitizes the dog but man is infected from swallowing cyclops which carries the parasite in drinking water *Strongyloides stercoralis* passes directly through the skin from moist soil Neither of the last two are found in the United States

THE CAT

Cats enjoy an intimate contact with the human family Because of prolific breeding and the mistaken sympathy of some persons which allows cats to wander homeless instead of being destroyed the number of such animals in the country is numerous

Table 63—Diseases Transmitted from Dog to Man

Disease	Etiologic Agent	Method of Human Infection
Boutonneuse fever	*Rickettsia conori*	By tick bite
Brazilian typhus	*Rickettsia rickettsi*	By tick bite
Brucellosis	*Brucella abortus*	
	Brucella melitensis	
	Brucella suis	By contact
Choriomeningitis lymphocytic	Filtrable virus	Method uncertain possibly by ticks
Coccidioidomycosis	*Coccidioides immitis*	By inhalation and through skin abrasion
Colombian typhus	*Rickettsia rickettsi*	By tick bite
Kenya typhus	*Rickettsia conori*	By tick bite
Leptospirosis	*Leptospira canicola*	
	L icterohaemorrhagiae	Through skin abrasions
Rabies	Filtrable virus	By dog bite
Ringworm	*Microsporum felineum*	By contact
	Tinea circinata	By contact
Rocky Mountain spotted fever	*Rickettsia rickettsi*	By tick bite
South African tick fever	*Rickettsia pijperi*	By tick bite
Sporotrichosis	*Sporotrichum schenckii*	Through skin abrasions
Tuberculosis	*Mycobacterium tuberculosis* var *bovis*	By contact
	Mycobacterium tuberculosis var *hominis*	By contact
Tularemia	*Pasteurella tularensis*	Through skin abrasions and by tick bite
Animal Parasites		
Amebiasis	*Endamoeba histolytica*	From food and drinking water
Creeping Eruption	*Ancylostoma braziliense*	Through the skin
Dog tapeworm infection	*Dipylidium caninum*	From swallowing an infected flea
Dracontiasis	*Dracunculus medinensis*	From drinking water
Echinochasmus infection	*Echinochasmus perfoliatus*	From eating fresh water fish
Echinostoma infection	*Echinostoma ilocanum*	From eating fish
Fish tapeworm infection	*Diphyllobothrium latum*	From eating fish
Gnathostoma infection	*Gnathostoma spinigerum*	Method uncertain
Heterophydiasis	*Heterophyes heterophyes*	From eating fish
Hydatid diseases	*Echinococcus granulosus*	By swallowing parasite eggs from dog feces
Leishmaniasis (Kala azar)	*Leishmania donovani*	By sandfly bite probably
Leishmaniasis (Oriental sore)	*Leishmania tropica*	By sandfly bite probably
Lung fluke disease	*Paragonimus westermani*	From eating crayfish and crabs
Opisthorchiasis	*Clonorchis sinensis*	
	Opisthorchis felineus	From eating raw fish
Schistosomiasis	*Schistosoma japonicum*	Through the skin
Strongyloidiasis	*Strongyloides stercoralis*	Through the skin
Thelazia infection	*Thelazia californiensis*	
	Thelazia callipaeda	Method uncertain
Trypanosomiasis American	*Trypanosoma cruzi*	By assassin bug bite

Dogs have been reported susceptible to the organism causing scarlet fever and free access of a dog to a human case of the disease might be a menace to children

A large number of animal parasites are found in dogs fifty nine

from fish The liver fluke *Opisthorchis felineus* is common in Europe while the closely related species *Opisthorchis pseudofelineus* is found in the central part of the United States The Chinese liver fluke *Clonorchis sinensis* is also closely related but not found in the United States These parasites are natural inhabitants of the cat but man is usually infected from eating fish that carry the parasites

Table 64.—DISEASES TRANSMITTED FROM CAT TO MAN

DISEASE	ETIOLOGIC AGENT	METHOD OF HUMAN INFECTION
Rabies	Filtrable virus	By cat bite
Ringworm	*Microsporum felineum*	By contact
	Tinea circinata	By contact
	Achorion schoenleinii	By contact
Tuberculosis	*Mycobacterium tuberculosis* var *bovis*	By contact
Animal Parasites		
Amebiasis	*Endamoeba histolytica*	From contaminated food and drinking water
Creeping eruption	*Ancylostoma braziliense*	Through the skin
Dog tapeworm infection	*Dipylidium caninum*	From swallowing an infected flea
Echinostoma infection	*Echinostoma ilocanum*	From eating infected fish
Fish tapeworm infection	*Diphyllobothrium latum*	From eating infected fish
Gnathostoma infection	*Gnathostoma spinigerum*	Method uncertain
Heterophydiasis	*Heterophyes heterophyes*	From eating infected fish
Leishmaniasis (Kala azar)	*Leishmania donovani*	By sandfly bite probably
Lung fluke disease	*Paragonimus westermani*	From eating infected crayfish and crabs
Opisthorchiasis	*Opisthorchis felineus*	
	Opisthorchis pseudofelineus	
	Clonorchis sinensis	From eating infected fish
Schistosomiasis	*Schistosoma japonicum*	Through the skin
Strongyloidiasis	*Strongyloides stercoralis*	Through the skin
Thelazia infection	*Thelazia californicus*	Method uncertain

Other flukes which the cat harbors incidentally are the Oriental lung fluke *Paragonimus westermani* acquired by man from crayfish and crabs and the intestinal flukes *Echinostoma ilocanum* and *Heterophyes heterophyes* with which man is infected in the Orient by eating raw fish The blood fluke *Schistosoma japonicum* found in China and Japan infects cats but must pass part of its life in the snail before it infects man

The round worm *Trichinella spiralis* sometimes infects the cat which in turn is infected by the rat but man is infected with trichinosis from pork *Strongyloides stercoralis* is an intestinal parasite of the cat which passes directly through the skin from the soil in tropical climates

Rabies is not uncommon in cats because of the contact in the house with dogs The rabid cat is a serious menace especially to children

Three types of ringworm may be contracted from cats Ringworm of the scalp in children is caused by *Microsporum felineum* and ringworm of the glabrous skin by *Tinea circinata* Favus an infection of the scalp caused by *Achorion schoenleinii* is acquired from cats which in turn acquired it from rats

Cats are fairly resistant to most bacterial diseases On rare occasions they have been found suffering from bovine tuberculosis from infected milk or meat They are susceptible to glanders but rarely contract the disease naturally They have given positive agglutination tests for brucellosis on the Island of Malta and Bruce isolated *Brucella melitensis* from the mesenteric glands of five such infected animals They may carry the organisms of tularemia and rat bite fever mechanically on their teeth after feeding on other infected animals and several human cases of each disease have been reported following a cat bite They harbor the spirochetes of leptospirosis from eating infected rats Their relation to diphtheria is in doubt but Simmons reports two cats from which he obtained diphtheria bacilli One instance has been reported where five cases of endemic typhus fever were acquired from kittens The cat flea *Ctenocephalides felis* harbored the virus (2)

Animal parasites are common in cats Among the protozoa there are three that deserve mention *Endamoeba histolytica* is found but the cat is probably of small significance in the epidemiology of amebic dysentery compared with other methods *Trypanosoma cruzi* is carried by cats in South America and *Leishmania donovani* in southern Europe and Asia and northern Africa

Monnig lists thirty seven helminths found in cats a considerable number of which infect man Several are found in the United States Creeping eruption caused by *Ancylostoma braziliense* is present in the southeastern part of the country Cats should be kept from bathing beaches and other places where people go barefoot The dog tapeworm *Dipylidium caninum* is acquired from the cat by swallowing a flea which has taken up the tapeworm egg Children are the chief sufferers but the disease is relatively uncommon Another tapeworm in the Great Lakes region of the United States *Diphyllobothrium latum* finds a reservoir in the cat but man is infected

times these migrations include hundreds of rats traveling together

The black rat or English rat *Rattus rattus rattus* has been known in Europe since the twelfth century It appeared in North America in the sixteenth century where it was the common rat among the early settlers Later it was supplanted to a large degree by the more ferocious and more prolific brown rat At the present time its range in this country is confined to certain areas in the southern states where it finds a warmer climate more to its liking The black rat is a great sea traveler breeding in the walls of cargo vessels In some instances as many as 99 5 per cent of rats on a ship are black rats It is a good climber and finds its habitat in the upper stories of build ings The black rat was the cause of plague in the middle ages

The roof rat or Alexandrian rat *Rattus rattus alexandrianus* was supposed to have originated in Egypt It is closely related to the black rat the chief difference being that of color (tawny black or gray) It is not numerous in the United States but may be found in the semitropical portions of the southern states Like the black rat the roof rat is a great climber and often nests in trees It may be found on ships also

The common house mouse *Mus musculus* found its way to Amer ica with the earliest settlers It has been able to hold its own with the brown rat because of its ability to escape into retreats too small for the rat to follow The distinction between rats and mice is arbi trary the main point of difference being size

Field rats and field mice in the United States are numerous and are of importance from the economic standpoint in destroying crops They are of lesser significance as far as disease is concerned al though potential sources of danger

The number of rats is estimated to equal the human population in the United States They are not of course distributed evenly and some communities will be badly infested while others which have waged anti rat campaigns will be relatively free The same is true of farms In cities it is estimated that the rat population is de creasing due to eternal vigilance

The cost of maintaining rats is estimated to be about two dollars per rat per year or approximately $250 000 000 00 It varies from fifty cents each per annum on farms to five dollars each in hotels Rats go into the fields to destroy the crops before they are harvested they breed enormously in storehouses and warehouses and ships to feed upon any merchandise available they damage the buildings in

THE RAT AND MOUSE

The domestic rat—domestic in the sense that it makes its abode with man—is the most useless of all animals There is nothing to say in its favor there are numerous reasons why it should be exterminated As a marauder it has taken heavy toll of farmer and merchant and householder as a murderer it has destroyed millions of innocent persons Among the animals it is man s public enemy number one Rats were present in Europe in the Pliocene period as indicated by fossil remains the lake dwellers during the glacial period in Europe knew it the Philistines made golden images of them the Romans pictured them on coins Greek Roman and Etruscan works of art show them at various occupations such as gnawing the ropes of ships or feeding on mussel beds from Palestine and Italy ancient bronze and terra cotta works indicate the presence of rats

There are hundreds of different species of rats and mice in different parts of the world Some are found in human dwellings and others in the field or forest In different parts of the globe different types of house rats are encountered and in most countries more than one type is present Their importance as disease carriers varies according to the morphologic and biologic type

The brown rat *Rattus norvegicus* also called the Norway rat sewer rat wharf rat and barn rat is supposed to be of Asiatic origin It appeared in Europe early in the eighteenth century and reached North America about the time of the American Revolution probably being brought from England as an accidental passenger (it is not a natural inhabitant of ships as are the black rat and the roof rat) It is now the most common species in the United States It is larger and more ferocious than the black rat or roof rat and has driven out those species in many places It has made its home in houses and farms in the country and in warehouses and about markets and wharfs in the city It lacks ability to climb to any extent and lives in the ground in excavations or under floors It often uses the sewers in cities for highways hence the name sewer rat It breeds prolifically the female after a gestation period of twenty one days giving birth to a dozen or more young From three to five litters a year occur usually during the warm months of the year Some females however may produce more litters and it is not uncommon to find young rats in cold weather It is a great traveler migrating from building to building and from farm to farm Some-

shown to harbor various types of Salmonella organisms in their intestines Choriomeningitis may possibly be transmitted to man from the rat through food but the epidemiology of the disease is obscure

Leptospirosis in rats is common the spirochetes being acquired by man through skin lesions either directly from the rat or from contaminated water Tularemia in rats is seldom found in the United States but elsewhere large epidemics have resulted from handling infected such rodents Ringworm and sporotrichosis sometimes are acquired from rats through skin lesions or by contact

Poliomyelitis virus has been encountered in rats and mice occasionally but the epidemiology of the disease probably does not include these animals

The several animal parasites which afflict rats are not of great epidemiologic importance Food contaminated by rat droppings may contain eggs of the rat tapeworm or the dwarf tapeworm *Endamoeba histolytica* is likewise conveyed to man through such contaminated food or drinking water The rat suffers from trichinosis and may possibly infect the hog from which man receives his infection *Trypanasoma cruzi* has been found in rats in California but no human cases of trypanosomiasis have been traced to such rodents

THE HEN AND OTHER BIRDS

Poultry is the most numerous of all livestock on the farms In 1940 there were about 338 000 000 hens in the United States Receipts from poultry and eggs exceed a billion dollars annually

The domestic fowl is assuming increasing importance as a carrier of human disease The viruses of equine encephalomyelitis and St Louis encephalitis which infect horses and man find a natural reservoir in the hen Swine erysipelas is a disease of hogs but the causative agent *Erysipelothrix rhusiopathiae* is carried by hens to hogs Poultry is naturally infected with *Brucella abortus* and *Br suis* in the United States and with *Br melitensis* in France making the control of brucellosis in the cow hog and goat more difficult Many types of *Salmonella* bacteria are found in poultry and according to Barnes the domestic fowl is the main reservoir of such organisms affecting man *Salmonella typhimurium* the most common cause of Salmonella food poisoning in man is found more frequently in hens than in all other animals combined *S pullorum* is a serious disease in chickens but human infections are rare although some have been

which they live by making holes in walls and foundations they destroy poultry and eggs and attack livestock upon occasion The United States Department of Agriculture reports cases where rats gnawed the feet of elephants gnawed holes in the bellies of fat hogs and killed young lambs

There are nearly a score of human diseases carried by rats most of which are found in the United States (table 65) The most serious

Table 65—DISEASES TRANSMITTED FROM RATS AND MICE TO MAN

DISEASE	ETIOLOGIC AGENT	METHOD OF HUMAN INFECTION
Choriomeningitis lymphocytic	Filtrable virus	Method uncertain
Haverhill fever	*Streptobacillus moniliformis*	By rat bite and from milk
Histoplasmosis	*Histoplasma* organisms	By contact
Leptospirosis	*Leptospira icterohaemorrhagiae*	Through skin abrasions
Plague	*Pasteurella pestis*	By flea bite
Q fever	*Rickettsia burneti*	By tick bite
Rat bite fever	*Spirillum minus*	By rat bite
Relapsing fever (endemic)	*Borrelia* spirochetes	By tick bite
Ringworm	*Achorion schoenleinii*	
	Achorion quinckeanum	By contact
Salmonella food infection	*Salmonella* bacteria	From contaminated food
Sporotrichosis	*Sporotrichum schenckii*	Through skin abrasions
Tsutsugamushi disease	*Rickettsia orientalis*	By mite bite
Tularemia	*Pasteurella tularensis*	Through skin abrasions
Typhus Fever (murine)	*Rickettsia mooseri*	By flea bite
Animal Parasites		
Amebiasis	*Endamoeba histolytica*	From food and drinking water
Dwarf tapeworm infection	*Hymenolepis nana*	From contaminated food
Lung fluke disease	*Paragonimus westermani*	From eating crayfish and crabs
Rat tapeworm infection	*Hymenolepis diminuta*	From swallowing infected insect
Trichinosis	*Trichinella spiralis*	From pork product
Trypanosomiasis (American)	*Trypanosoma cruzi*	By assassin bug bite

is plague transmitted by the rat flea Eternal vigilance by public health authorities has prevented the spread of plague in rats in the United States but it is always a potential danger (sylvatic plague is found in ground squirrels in many western states) Other diseases transmitted by the ectoparasites of rats are murine typhus fever by flea bite and tsutsugamushi disease or mite typhus by mites (the latter is found only in the Orient and adjacent territory) Endemic relapsing fever is transmitted by ticks

Rat bite fever and Haverhill fever are caused by rat bites In one epidemic Haverhill fever resulted from milk possibly contaminated by rats Salmonella food infections often result from food to which rats have had access Rats in many parts of the country have been

sipelas and of brucellosis Ducks carry the virus of ornithosis as well as a tapeworm *Drepanidotaenia lanceolata* which occasionally infects man Pigeons are more or less commonly infected with the virus of ornithosis (psittacosis) and are perhaps a serious menace Pigeons likewise carry *Erysipelothrix rhusiopathiae* the cause of swine erysipelas

The psittacine birds such as parrots parrakeets parrotlets cockatoos and related species both in the domestic and wild states are of consequence because of psittacosis The virus is exceedingly virulent for man who is infected by contact with such birds Parrots in captivity are susceptible to the various types of tuberculosis human bovine and avian and are capable of infecting persons who live where such birds are kept

Wild birds of many kinds act as reservoirs for the viruses of equine encephalomyelitis as well as of St Louis encephalitis the disease being transmitted to the horse or to man by the mosquito or other insect Tularemia is found in various wild game birds such as the grouse quail or sage hen but the virulence of *Pasteurella tularensis* seems to be lower for man when coming from such sources Wild birds sometimes act as mechanical carriers of infection such as anthrax after feeding on dead animals

WILD ANIMALS AND GAME

Many wild animals harbor agents of disease with which man might become infected but contact with man is so remote that comparatively few infections take place

The monkey is subject to most of the ills of mankind In its wild state it carries the virus of jungle yellow fever transmitted by mosquitoes and relapsing fever transmitted by ticks Plague is rare in the monkey but does sometimes occur Tuberculosis is found only in monkeys in captivity The various animal parasites which are carried by monkeys include those which cause amebiasis balantidiasis schistosomiasis ternidens infection and American trypanosomiasis (Chagas disease) An epidemic in baboons due to *Salmonella typhimurium* was reported by Scott An epidemic in chimpanzees was studied by Wilbert in which he found spirochetes similar to *Leptospira icterohaemorrhagiae*

There have been several reports of trichinosis from the consumption of bear meat infected with *Trichinella spiralis* The bear also harbors the virus of Rocky Mountain spotted fever as does the

reported The egg as well as the flesh may contain the organisms Ornithosis (psittacosis) in the domestic fowl is assuming an increasingly important role in the epidemiology of that disease Avian tuberculosis very rarely finds a human victim Diphtheria has been reported in poultry, the infection coming from human cases but such instances are probably uncommon Listerellosis occurs as a systemic disease of chickens but how man is infected is uncertain The fowl mite *Dermanyssus gallinae*, causes an itchy dermatitis on the hands of poultry attendants

Table 66—DISEASES TRANSMITTED BY POULTRY AND OTHER BIRDS TO MAN

DISEASE	ETIOLOGIC AGENT	METHOD OF HUMAN INFECTION
Domestic Fowl		
Brucellosis	*Brucella abortus* *Brucella melitensis* *Brucella suis*	By contact
Encephalitis St Louis type	Filtrable virus	By mosquito bite
Encephalomyelitis equine	Filtrable virus	By mosquito bite
Listerellosis	*Listerella monocytogenes*	Method in doubt
Ornithosis	Filtrable virus	By contact
Salmonella food infections	*Salmonella* bacteria	From poultry and eggs
Swine erysipelas	*Erysipelothrix rhusiopathiae*	Through skin abrasions
Duck		
Duck tapeworm infection	*Drepanidotaenia lanceolata*	By mouth
Echinostoma infection	*Echinostoma revoltum*	From molluscs
Ornithosis	Filtrable virus	By contact
Pigeon		
Ornithosis	Filtrable virus	By contact
Swine erysipelas	*Erysipelothrix rhusiopathiae*	Through skin abrasions
Turkey		
Brucellosis	*Brucella abortus* *Brucella melitensis* *Brucella suis*	By contact
Swine erysipelas	*Erysipelothrix rhusiopathiae*	Through skin abrasions
Psittacine Birds		
Psittacosis	Filtrable virus	By contact
Tuberculosis (human type)	*Mycobacterium tuberculosis hominis*	By contact
Wild Game Birds		
Encephalitis St Louis type	Filtrable virus	By mosquito bite
Encephalomyelitis equine	Filtrable virus	By mosquito bite
Tularemia	*Pasteurella tularensis*	Through skin abrasions

Other domestic birds also act as reservoirs of disease that may be carried to man Turkeys are of importance as carriers of swine ery

Table 6 —REVIEW OF DISEASES WHICH ANIMALS TRANSMIT TO MAN WITH THE ANIMAL HOSTS

DISEASE	ETIOLOGIC AGENT	COMMON ANIMAL HOST	USUAL METHOD OF HUMAN INFECTION
Actinomycosis	*Actinomyces bovis*	Cow, horse, sheep, hog, goat, dog, wild animals	Method in doubt
Amebiasis	*Endamoeba histolytica*	Rat, dog, cat, monkey	From contaminated food and drinking water
Amphistomiasis	*Amphistoma hominis*	Hog	From contaminated food and drinking water
Anthrax	*Bacillus anthracis*	Cow, horse, sheep, goat, wild animals	By contact, hair and hides
Balantidiasis	*Balantidium coli*	Hog	From contaminated food and drinking water
Beef tapeworm infection	*Taenia saginata*	Cow	Insufficiently cooked beef
Botulism	*Clostridium parabotulinum*	Intestines of many animals	Through home-canned foods
Boutonneuse fever	*Rickettsia conori*	Dog	By tick bite
Brazilian typhus	*Rickettsia rickettsi*	Dog	By tick bite
Brucellosis	*Brucella abortus*, *Br. melitensis*, *Br. suis*	Goat, cow, hog, sheep, horse, dog, hen, turkey	Through milk and by contact
Choriomeningitis, lymphocytic	Filtrable virus	Mouse	Probably through food and from dust
Coccidioidomycosis	*Coccidioides immitis*	Rodents, dog, cow, sheep	By inhalation and through wound
Colombian typhus	*Rickettsia rickettsi*	Dog	By tick bite
Contagious ecthyma of sheep	Filtrable virus	Sheep	Probably through skin abrasion
Cowpox	Filtrable virus	Cow	Through skin abrasions and by vaccination
Creeping eruption	*Ancylostoma braziliense*	Dog, cat	Through the unbroken skin
Diphtheria	*Corynebacterium diphtheriae*	Cow	Through milk
Dog tapeworm infection	*Dipylidium caninum*	Dog, cat	From swallowing infected fleas
Dracontiasis	*Dracunculus medinensis*	Dog, cow, fur bearing animals	From drinking water
Dwarf tapeworm infection	*Hymenolepis nana*	Rat, mouse	From contaminated food
Echinochasmus infection	*Echinochasmus perfoliatus*	Dog	From eating fresh water fish
Echinostoma infection	*Echinostoma ilocanum*	Cat, dog, hog	From eating infected fish
Echinostoma infection	*Echinostoma revolutum*	Duck	From molluscs

Rocky Mountain sheep the mountain lion the wildcat the badger and many other wild animals Deer suffer from anthrax and foot and mouth disease acquired from cattle Tularemia is acquired from rabbits Trypanosomiasis in Africa (African sleeping sickness) finds a reservoir in antelope trypanosomiasis in America (Chagas disease) finds residence in the bat armadillo and opossum but in the United States no human cases have been reported from such infected animals The armadillo and the opossum likewise are reservoirs of Rocky Mountain spotted fever and endemic relapsing fever The coyote and the fox suffer from rabies making it difficult to eradicate the disease in dogs Occasionally they may be infected with tularemia

Wild rodents are responsible for several diseases The ground squirrel is the reservoir of sylvatic plague in western United States but other carriers include chipmunks prairie dogs marmots pocket mice white footed mice meadow mice wood rats and rabbits Rabbits are the chief cause of tularemia in man but the etiologic agent of the disease is found in ground squirrels tree squirrels prairie dogs woodchucks muskrats and chipmunks Chipmunks also harbor the spirochetes of endemic relapsing fever

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Table 67 Continued

Disease	Etiologic Agent	Common Animal Host	Usual Method of Human Infection
Opisthorchiasis (Cont.)	*Opisthorchis felineus*	Dog, cat, other animals	From eating raw fish
Ornithosis (Psittacosis)	Filtrable virus	Psittacine bird, hen, pigeon, ducks	By contact
Plague	*Pasteurella pestis*	Rat and other rodents	By flea bite
Pork tapeworm infection	*Taenia solium*	Hog	From insufficiently cooked pork
Q fever	*Rickettsia burneti*	Bandicoot, rat, cow, sheep	By tick bite
Rabies	Filtrable virus	Dog, wolf, coyote, other animals	Dog bite, sometimes other animal bites
Rat bite fever	*Spirillum minus*	Rat	By rat bite
Rat tapeworm infection	*Hymenolepis diminuta*	Rat, mouse	From swallowing infected insect
Relapsing fever, endemic	Spirochetes, genus *Borrelia*	Wild rodents and other animals	By tick bite
Rift Valley fever	Filtrable virus	Cattle and sheep	Mosquito bite
Ringworm	*Achorion quinckeanum*	Rat	By contact
	Achorion schoenleinii	Cat, rat, dog	By contact
	Microsporum felineum	Cat, dog	By contact
	Tinea barbae	Cow, horse	By contact
	Tinea capitis	Dog, cow	By contact
	Tinea circinata	Cat, dog, horse, cow, monkey	By contact
Rocky Mountain spotted fever	*Rickettsia rickettsi*	Wild rodents and other animals	By tick bite
Russian spring summer fever	Filtrable virus	Wild rodent	By tick bite
Salmonella food infections	*Salmonella* bacteria	Cow, hog, hen, sheep, rat	Infected meat and food contaminated by rat droppings
Sarcocystiasis	*Sarcocystis* species	Cow, sheep, horse, hog, rabbit, mouse	From contaminated food and water
Scarlet fever	*Streptococcus pyogenes* (*St. scarlatinae*)	Cow	From milk
Schistosomiasis	*Schistosoma japonicum*	Dog, cat, cow, other animals	Through the skin
Schistosomiasis	*Sch. mansoni*	Monkey	Through the skin
Sheep wireworm infection	*Haemonchus contortus*	Sheep, goat, cow	From drinking water
South African tick fever	*Rickettsia pijperi*	Dog	By tick bite

Table 67 Continued

Disease	Etiologic Agent	Common Animal Host	Usual Method of Human Infection
Encephalitis Japanese B type	Filtrable virus	Birds rodents	By mosquito bite
Encephalitis St Louis type	Filtrable virus	Hen other birds and animals	By mosquito bite
Encephalomyelitis equine	Filtrable virus	Hen horse other birds and animal	By mosquito bite
Fascioliasis	*Fasciola hepatica*	Sheep cow other herbivorous animals	From raw plant food
Fasciolopsis infection	*Fasciolopsis buski*	Hog	From raw plant foods
Fish tapeworm infection	*Diphyllobothrium latum*	Dog cat wild carnivores	From eating fish
Foot and mouth disease	Filtrable virus	Cow and other cloven footed animals	By contact and through milk
Gas gangrene	*Clostridium perfringens* and others	Intestines of many animals	Through wounds
Glanders	*Malleomyces mallei*	Horse mule and donkey	By contact
Gnathostoma infection	*Gnathostoma spinigerum*	Dog cat	Method uncertain
Gnathostoma infection	*Gnathostoma hispidum*	Hog	Method uncertain
Haverhill fever	*Streptobacillus moniliformis*	Rat	By rat bite and from milk
Heterophyidiasis	*Heterophyes heterophyes*	Dog cat	From eating fish
Histoplasmosis	*Histoplasma capsulatum*	Horse	Probably by contact
Hydatid disease	*Echinococcus granulosus*	Dog cow sheep hog other animals	By swallowing parasite eggs from dog feces
Kenya typhus	*Rickettsia conori*	Dog	By tick bite
Leishmaniasis Kala azar	*Leishmania donovani*	Dog	Probably by sand fly bite
Leishmaniasis Oriental sore	*Leishmania tropica*	Dog	Probably by sand fly bite
Leptospirosis	*Leptospira canicola*	Dog	Through skin abrasions
Leptospirosis	*L. icterohaemorrhagiae*	Rat dog	Through skin abrasions
Listerellosis	*Listerella monocytogenes*	Cow sheep hen other animals	Method uncertain
Louping ill	Filtrable virus	Sheep	Method uncertain
Lung fluke disease	*Paragonimus westermani*	Hog dog cat wild animals	From eating crayfish and crab
Lungworm infection	*Metastrongylus elongatus*	Hog sheep cow	By mouth
Milkers nodules	Probably a virus	Cow	By contact
Milk sickness	A chemical poison	Cow	From milk
Opisthorchiasis	*Clonorchis sinensis*	Dog cat hog wild animals	From eating raw fish

Table 67 Continued

Disease	Etiologic Agent	Common Animal Host	Usual Method of Human Infection
Opisthorchiasis (Cont.)	*Opisthorchis felineus*	Dog, cat, other animals	From eating raw fish
Ornithosis (Psittacosis)	Filtrable virus	Psittacine bird, hen, pigeon, ducks	By contact
Plague	*Pasteurella pestis*	Rat and other rodents	By flea bite
Pork tapeworm infection	*Taenia solium*	Hog	From insufficiently cooked pork
Q fever	*Rickettsia burnetii*	Bandicoot, rat, cow, sheep	By tick bite
Rabies	Filtrable virus	Dog, wolf, coyote, other animal	Dog bite, sometimes other animal bite
Rat bite fever	*Spirillum minus*	Rat	By rat bite
Rat tapeworm infection	*Hymenolepis diminuta*	Rat, mouse	From swallowing infected insects
Relapsing fever endemic	Spirochete, genus *Borrelia*	Wild rodents and other animals	By tick bite
Rift Valley fever	Filtrable virus	Cattle and sheep	Mosquito bite
Ringworm	*Achorion quinckeanum*	Rat	By contact
	Achorion schoenleinii	Cat, rat, dog	By contact
	Microsporum felineum	Cat, dog	By contact
	Tinea barbae	Cow, horse	By contact
	Tinea capitis	Dog, cow	By contact
	Tinea circinata	Cat, dog, horse, cow, monkey	By contact
Rocky Mountain spotted fever	*Rickettsia rickettsi*	Wild rodents and other animals	By tick bite
Russian spring summer fever	Filtrable virus	Wild rodents	By tick bite
Salmonella food infection	*Salmonella* bacteria	Cow, hog, hen, sheep, rat	Infected meat and food contaminated by rat droppings
Sarcocystiasis	*Sarcocystis* species	Cow, sheep, horse, hog, rabbit, mouse	From contaminated food and water
Scarlet fever	*Streptococcus pyogenes* (*St. scarlatinae*)	Cow	From milk
Schistosomiasis	*Schistosoma japonicum*	Dog, cat, cow, other animals	Through the skin
Schistosomiasis	*Sch. mansoni*	Monkey	Through the skin
Sheep wireworm infection	*Haemonchus contortus*	Sheep, goat, cow	From drinking water
South African tick fever	*Rickettsia pijperi*	Dog	By tick bite

Table 67 Continued

Disease	Etiologic Agent	Common Animal Host	Usual Method of Human Infection
Sporotrichosis	*Sporotrichum schenki*	Horse rat dog	Through skin abrasions
Streptococcus sore throat	*Streptococcus pyogenes* (*St epidemicus*)	Cow	From milk
Strongyloidiasis	*Strongyloides stercoralis*	Dog cat	Through the skin
Swine erysipelas	*Erysipelothrix rhusiopathiae*	Hog hen turkey	Through skin abrasion
Syngamus infection	*Syngamus laryngeus*	Cow goat water buffalo	By mouth
Ternidens infection	*Ternidens diminutus*	Monkey	Probably by mouth
Tetanus	*Clostridium tetani*	Intestine of horse and other animals	Through skin abrasions
Thelazia infection	*Thelazia californiensis*	Dog cat	Method uncertain
Thelazia infection	*Thelazia callipaeda*	Dog	Method uncertain
Toxoplasmosis	*Toxoplasma* species	Rodent birds	Method uncertain
Trichinosis	*Trichinella spiralis*	Hog rat	From insufficiently cooked pork
Trichostrongylus	*Trichostrongylus* species	Cow sheep goat other herbivorous animals	From food or water
Trypanosomiasis African	*Trypanosoma gambiense* and *Tr rhodesiense*	Antelope cow sheep horse	By tsetse fly bite
Trypanosomiasis American	*Trypanosoma cruzi*	Armadillo opossum bat monkey rodent dog cat	By assassin bug bite
Tsutsugamushi disease	*Rickettsia orientalis*	Field rats and mice	By mite bite
Tuberculosis avian	*Mycobacterium tuberculosis* var *avium*	Hen hog wild birds in captivity	Human infections very rare
Tuberculosis bovine	*M tuberculosis* var *bovis*	Cow hog dog goat cat horse	Infected milk or meat or by contact
Tuberculosis human	*M tuberculosis* var *hominis*	Hog dog	From pork or by contact
Tularemia	*Pasteurella tularensis*	Rabbit other animals and wild birds	Through skin abrasions or tick bite
Typhus fever murine	*Rickettsia mooseri*	Rat	By flea bite
Yellow fever jungle type	Filtrable virus	Wild animals	By mosquito bite

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